Ministry of Tribal Affairs,
Government of India

icmr INDIAN COUNCIL OF MEDICAL RESEARCH | RMRCBB REGIONAL MEDICAL RESEARCH CENTRE, BHUBANESWAR.

SCSTRTI
ST & SC Development, Minorities & Backward Classes Welfare Department, Govt. of Odisha.

Mapping of Sickle Cell Anaemia in the Tribal Sub-Plan Area among the Tribal Communities of the State and a Compendium of Empirical Studies & its findings on Sickle Cell Anaemia among the Tribal Communities of Odisha

A Joint initiative

By

SCs & STs Research & Training Institute, Bhubaneswar

and

ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha.

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Government of India

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PREFACE

Sickle cell anaemia is the most common monogenetic disorder currently prevailing worldwide. Prevalence of the disease is high among the people of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean. Sickle Cell Disease (SCD) is one of the neglected health problems in India. Since the early 20th century, scientific and clinical research on sickle cell disease has resulted in creation of a vast repository of scientific evidence on the disease. In the Indian context, significant research leads have been there on the disease guiding the programmatic directions towards abating sickle cell anaemia in the states and the country.

This report sets out to review the state of the art of research in the field of sickle cell anaemia in India, and to consider how existing research-based information contained in the publications can influence policy formulation and managerial decision-making towards abating sickle cell anaemia in tribal areas, especially in Odisha. The sickle gene is widespread in tribal populations in most of the tribal dominated states of the country towards which sickle cell anaemia control programs and initiatives have been operating in different states. In this context, this 'compendium of evidence' is an initiative towards contributing to the information need of policy makers and implementers by compiling, summarizing and analysing empirical studies on sickle cell disease in India.

Mapping of Sickle cell pockets in Odisha through GIS mapping helps in visualizing the state. The various blocks of Tribal sub plan areas districts have high burden of sickle cell cases, and this report has documented the sickle cell disease and sickle cell trait in Odisha.

The motivation for this report is that – in different ways – policymakers, managers, politicians and the general public have profound concerns about the efficiency of the initiatives taken towards addressing the increasing load of sickle cell anaemia. The contents in this report may be useful for improving policy and managerial decisions to control and abate sickle cell anaemia.

We therefore hope that it provides a solid foundation for conceptualizing interventions in the sickle cell anaemia sector and related health systems and offers a good basis for those seeking to take concrete actions.

ACKNOWLEDGEMENT

This **Research Project** would not have been possible without the financial support of the Ministry of Tribal Affairs (MoTA), Government of India. While expressing gratitude to MoTA, we express our humble appreciation to the leadership of Smt. Ranjana Chopra, IAS, Principal Secretary, ST & SC Development, Minority and Backward Classes Welfare Department, Government of Odisha for her visionary leadership and encouragement for taking up this innovative compilation.

In bringing out this Report in the field of Sickle Cell Anaemia, I am indebted to the team of researchers, specialists, reviewers and design experts who worked relentlessly and collaboratively at Regional Medical Research Centre (RMRC), Bhubaneswar and at SCSTRTI, Bhubaneswar to make it possible.

We are especially indebted to Prof. (Dr.) A. B. Ota, IAS (R), Advisor-cum-Director & Special Secretary to Govt. SCSTRTI, Bhubaneswar for his expert guidance and to his team members from SCSTRTI, Bhubaneswar. We are grateful to Dr. Bigyanananda Mohanty, Deputy Director and Ms. Moushumi Nayak, Assistant Director (R) who have been the coordinating links between RMRC and SCSTRTI for this project and contributing to the compilation on several counts. We are grateful to other staff of SCSTRTI, Bhubaneswar for their meaningful involvement without which this outcome would not have been as cherished.

We also take this opportunity to express a deep sense of gratitude to Dr. Sanghamitra Pati for her expert guidance and to her team members comprising Dr. Jaya Singh Kshatri, Scientist C; Dr. Asit Mansingh, Project Scientist C; Dr. Trilochan Bhoi, Research Assistant; at RMRC Bhubaneswar for undertaking the stupendous task of meticulously reviewing loads of the research results relevant to the studies on sickle cell anaemia in India. I am also thankful to the Program Associates - Mr. Ashok Kumar Mahakud, Mr. Debashish Mishra and Dr. Salinee Panda for contributing their part in this herculean task.

We are also thankful to Dr P. K Mohanty, Project Coordinator, Odisha Sickle Cell Project (NHM) for helping in providing district and block level data for sickle cell.

CONTENTS

EXECUTIVE SUMMARY

Sickle cell anaemia is the most common monogenic disorder currently prevailing worldwide. The disorder is highly prevalent among the people of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean. In India, sickle cell disease (SCD) is a neglected health problem, which explains why general research is scarce in this sector. Recent studies on Sickle Cell Disease/Trait are extensive, and these reviews have summarised the regional and population prevalence based on several cross-sectional surveys. The disease's prevalence in socially disadvantaged populations, which already face barriers to health care and inequities, necessitates a health-systems approach that goes beyond describing the prevalence and clinical features and tries to identify actionable gaps in the contextual understanding of the disease. Aside from infectious diseases and chronic diseases, genetic disorders such as Sickle cell disease are emerging as serious public health issues in India. In its most severe form, the illness is linked to chronic, life-altering, and life-threatening disorders, as well as health complications that can lead to disability or death.

Due to the severity of the problem and the financial consequences of its management, appropriate control measures must be introduced urgently. The prevention strategies implemented for controlling the disease may be the primary or secondary methods. The primary preventive strategy is to identify the carriers and to avoid the marriage of carrier couples and the secondary prevention strategy is to use prenatal diagnostics to prevent the birth of the affected child. The challenge to control Sickle cell disorder is substantial and an integrated approach is required for both screening and management of the disorder.

The report is the outcome of the concerted efforts of the Regional Medical Research Centre, Bhubaneswar and Scheduled Castes and Scheduled Tribes Research and Training Institute, Bhubaneswar. The study is financed by the Ministry of Tribal Affairs (MoTA), Government of India. The objective of the study is to collate the knowledge and research in the Sickle cell field and provide guidance to all concerned in this sector.

The present report highlights all the research which are carried out in the field of sickle cell involving the Indian population and GIS map of sickle cell cases in Odisha. The objective of this compendium is to collect all the research in the field of sickle cell in one place where evidence-based research will help the health care providers, Government agencies and at the policy level to use this knowledge hub for the prevention and management of sickle cell disorders. The compendium of

Evidence will serve as an evidence-based research collection that will update on all current research topics within this field. For this compendium, we have searched four databases which include Medline via PubMed, Embase via Ovid, Cochrane Library-CENTRAL and ProQuest. We have formulated different search strategies for different databases. We found a total of 13650 articles after the removal of duplicates which we included for the initial title and abstract screening. After initial and comprehensive article screening, we found a total of 803 articles that were relevant to sickle cell among the population of Indian origin. After all, articles were screened we have divided the articles and studies into different themes. We have divided all the studies, articles and reviews into 6 different themes. We have categorized all the rest articles into the theme "Others". The main themes identified were Prevalence, Screening and Disorder, Treatment, Reviews, Case reports, Programs and Others. We found a total of 286 articles/studies which were related to the prevalence or burden of sickle cell in India. We found 88 studies related to Screening and Diagnosis of sickle cell disease. We found 60 articles related to the treatment of sickle cell disease or disorders as the topic. We have included reviews like Narrative reviews, systematic reviews, Overviews of reviews where we found 50 studies. There were 196 case reports on Sickle cell topics from various parts of the country. We found 12 articles that were related to sickle cell programs in India. After classification of different articles and studies into different themes we have categorized all other articles into the theme "Others", there were a total of 111 entries under this theme which included Authors perspectives, epidemiological studies, newspaper articles, letters to the editor, book chapters, conference papers etc were categorized. We have also included the GIS maps of TSP areas of 13 districts. The maps show burden in Odisha and different blocks across the districts. Highest cases are from Sundargarh (3007) followed by Kandhamal (2109).

The report is a compilation of all the available research on the subject of Sickle cell disease in India structured in such a manner that it will help in answering any concern of health care professionals. This report will serve as the foundation of knowledge for sickle cell-related research in India.

INTRODUCTION

Sickle cell anaemia is an important public health problem among the tribal communities of Odisha, which needs serious attention. In this current study, an empirical analysis was carried out on the sickle cell studies in India for creating a compendium of evidence. A narrative synthesis was carried out based on predefined reporting criteria. A synoptic report was made based on the GIS mapping of the prevalence of sickle cell disease and trait in tribal pockets of Odisha. A qualitative review was also carried out to assess the feasibility of registration and data management in the sickle cell portal of the ministry of tribal affairs.

The project consisted of three main objectives as listed below.

Objectives:

a. Systematic review of evidence synthesis of sickle cell anaemia from empirical studies undertaken on tribal communities of Odisha and India (Compendium of evidence).

b. GIS Mapping of the Sickle Cell Anaemia Pockets in the TSP Areas.

c. Building and piloting for feasibility of implementation of a minimum dataset and associated android applications necessary to prepare a prospective registry of sickle cell anaemia patients in Odisha belonging to tribal communities (Development of a Portal and application development to capture data pertaining to sickle cell anaemia patients from tribal communities).

d. Final report

SECTION-1

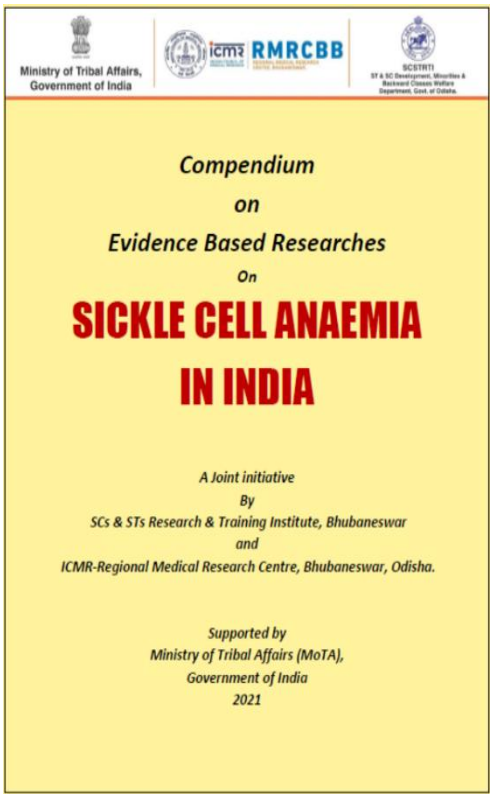
Objective

Systematic review of evidence synthesis of sickle cell anaemia from empirical studies undertaken on tribal communities of Odisha and India.

Summary

Sickle cell anaemia is the most common monogenic disorder currently prevailing worldwide. The disorder is highly prevalent among the people of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean. In India, sickle cell disease (SCD) is a neglected health problem, which explains why general research is scarce in this sector.

The report is the outcome of the concerted efforts of the Regional Medical Research Centre, Bhubaneswar and Scheduled Castes and Scheduled Tribes Research and Training Institute, Bhubaneswar. The study is supported by the Ministry of Tribal Affairs (MoTA), Government of India. The objective of the study is to collate the knowledge and research in the Sickle cell field and provide guidance to all concerned in this sector.

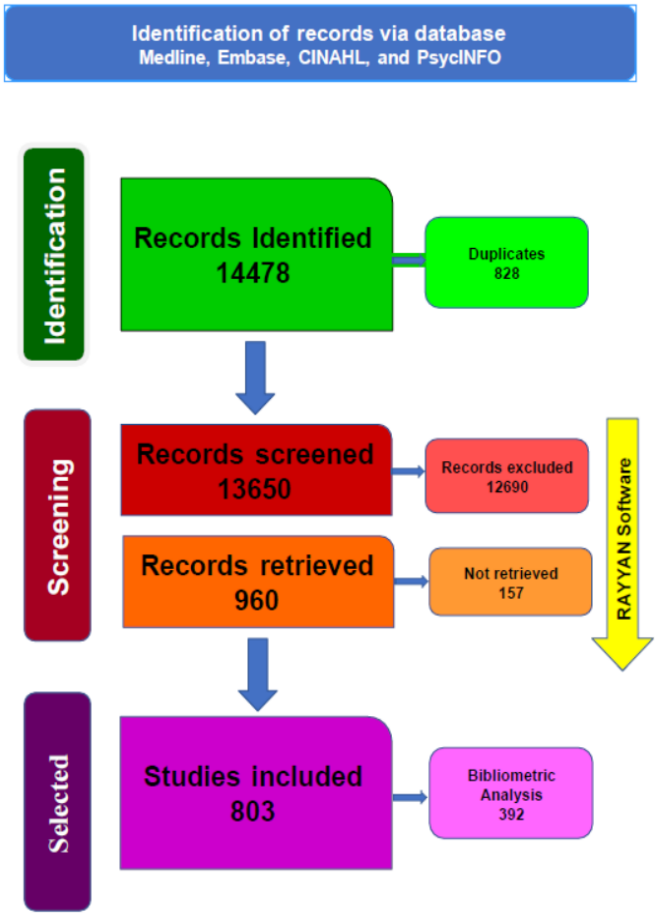


The present compendium of evidence highlights all the research which is carried out in the field of a sickle cells involving the Indian population. The objective of this compendium is to collect all the research in the field of sickle cell in one place where evidence-based research will help the health care providers, government agencies and the policy level to use this knowledge hub for the prevention and management of sickle cell disorders. The compendium is divided into different themes Prevalence of disease, Screening and Diagnosis of disease, Treatment for disease, Reviews related to Sickle cell, Case reports, Programs related to sickle cell and rest other studies.

This compendium will assist us in identifying knowledge gaps as well as link different works in the context of their contribution to the issue and other significant works in the same area. The report is a compilation of all the available

research on the subject of Sickle cell disease in India structured in such a manner that it will help in answering any concerns of health care professionals. This compendium of evidence will serve as the foundation of knowledge for sickle cell-related research in India.

Methodology



The analysis of empirical studies was carried out on sickle cell disease in India and a compendium of evidence report was made. A comprehensive systematic search of all available works of literature was performed using Medline, Embase, CINAHL, and PsycINFO databases. Information on study title, journal name, publication year, authorship, author's affiliations, study design, study setting, study site, and funding source was collected. Pre-defined criteria were used to screen all the available literature in the compendium and categorize them simultaneously into broad thematic groups. The screening and categorization were performed by using Rayyan software designed for this purpose. Descriptive statistics and cross-tabulations were performed using "R software ver. 4.0.3". A bibliometric analysis paper was registered in Open Science Framework (Reg. 10.17605/OSF.IO/6VXD3) on November 15, 2021. The articles were retrieved into a reference management software and checked for duplication. Following this, 2 authors each used pre-defined criteria to screen all the articles for inclusion into the compendium and categorize them simultaneously into the following broad thematic groups-

1. Prevalence of Sickle Cell Disease
2. Screening and Diagnosis
3. Treatment
4. Case-reports
5. Programs

6. Reviews
7. Others

Disagreements were resolved by discussion and consensus. The screening and categorization were performed by using Rayyan software designed for this purpose. A supervisor reviewed 10% of the articles to ensure consistency and maintain quality.

Key Findings

We found a total of 803 articles and case reports which included Sickle cell-related topics in the Indian context. We have divided all the screened articles into 7 subthemes

1. Prevalence- 286
2. Screening and Diagnosis- 88
3. Treatment- 60
4. Reviews- 50
5. Case report- 196
6. Programs- 12
7. Others- 111

Section-1 Prevalence

In the Prevalence theme, we found 286 articles and studies. We have included all the surveys, prevalence studies and cross-sectional studies under this theme. All the relevant records are added in the Compendium of evidence section. The records were further categorized in the Indian and Odisha context. The cross-sectional surveys/studies included in the theme mainly looks at the data from the population at a specific point of the time. The studies were observational in nature and the research carried out in these describe the characteristics existing in the community. These studies are often used to make inferences about possible relationships or to gather preliminary data to support further research and experimentation. We found a total of 286 records out of which 30 records were from Odisha.

Section-2 Screening and Diagnosis

In the screening and diagnosis theme, we found 88 articles. The articles were mainly addressed to prenatal and newborn screenings. In this section, records were included which were related to screening and diagnosis of Sickle cell condition in India. The screening studies included all the records which included methods, technique, procedure, and examination for early and rapid detection of sickle cell disease in the population. The diagnosis studies were records that included the process of identifying the disease, condition or injury from its sign and symptoms. This also included the process including health history, case history, physical examination and diagnostic tests such as blood tests, imaging tests and biopsies which all help in diagnosis. Out of total of 88 records we found 8 records related to Odisha.

Section-3 Treatment

We found 60 articles with the objective of treating or reducing any side effects from sickle cell disease. The records included in this theme were research studies performed in people that are aimed at evaluating a medical, surgical or behavioural intervention. The treatments used can help manage the disease. The use of medicine, therapy, surgery and other treatments helps in reducing the symptoms and effects of the disease. We found 5 studies from Odisha in this context.

Section-4 Reviews

The review articles are also known as literature reviews, it is a survey of previously published research on a topic. The overview of all the research to the particular research gives the critical evaluation of all the data from existing studies. The review articles identify potential research areas to explore and to draw new conclusions from existing data. We found a total of 50 reviews which included narrative reviews, systematic reviews, and overview of reviews.

Section-5 Case reports

An article that describes and interprets an individual case, often written in the form of a detailed story. Case reports often describe; Unique cases that cannot be explained by known diseases or syndromes; Cases that show an important variation of a disease or condition; Cases that show unexpected events that may yield new or useful information; Cases in which one patient has two or more unexpected diseases or disorders. Case reports are considered the lowest level of evidence, but they are also the first line of evidence because they are where new issues and ideas emerge. There were 196 case reports. The case reports were reported from individual patients. The individual reports were categorized under the case report's theme. From Odisha, we found 24 case reports.

Section-6 Programs

The theme Program includes research related to health programs related to sickle cell disease and which include individual and organizational level strategies and interventions that influences health. The program works as an informational approach directed towards change. We found 12 studies that were related to programs or projects related to sickle cell disease.

Section-7 Others

We have categorized all other articles, studies, abstracts and letters into the Others category. In the Others category, we have 111 publications which included case-control studies, Cohort studies, Abstracts, Epidemiology related studies, Letter to the editor, Perspectives, Clinical trials, News topics, Anthropology studies, Short communications, Pilot studies, Book chapters, Retrospective studies, Poems, Preliminary reports, Trade documents, Comments, Protocol papers, Perspectives, Observational study, Comorbidity study, Registry and Qualitative study.

The studies were again categorized into Odisha specific studies in which we found 73 studies. The distribution of studies is provided in the table below-

	Themes	Odisha	India
1	Prevalence	30	286
2	Screening and diagnosis	8	88
3	Treatment	5	60
4	Review	1	50
5	Case report	24	196
6	Programs	-	12
7	Others	5	111
	Total	73	803

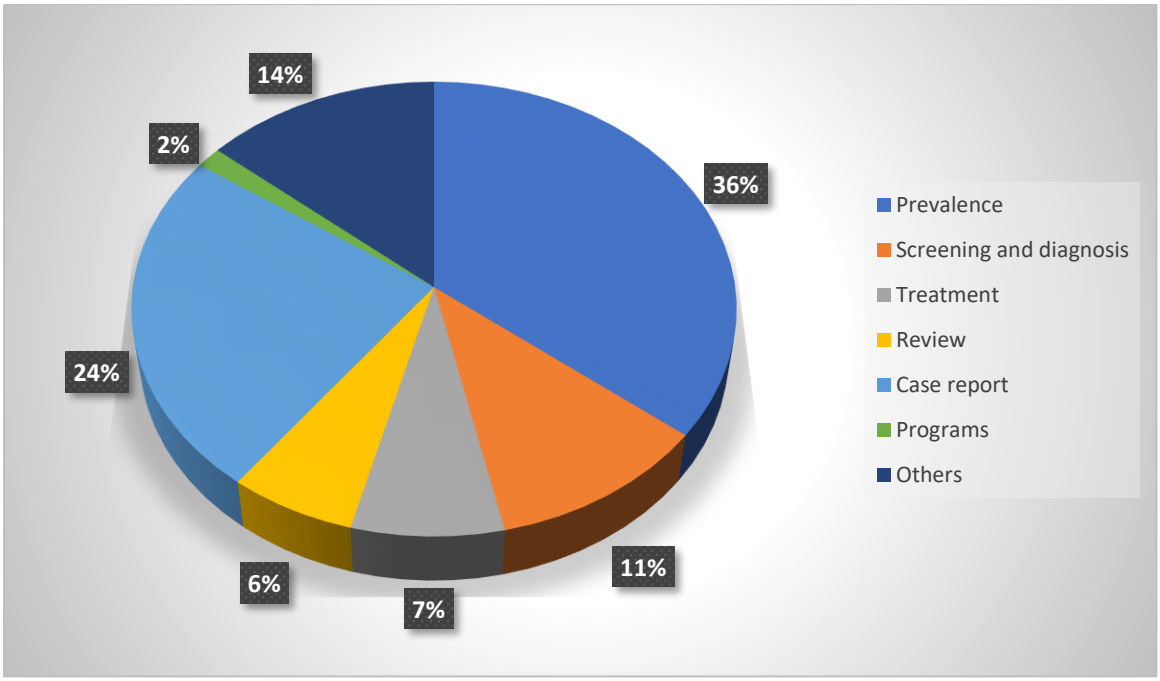


Figure 1- Thematic distribution of all publications relevant to the Indian population

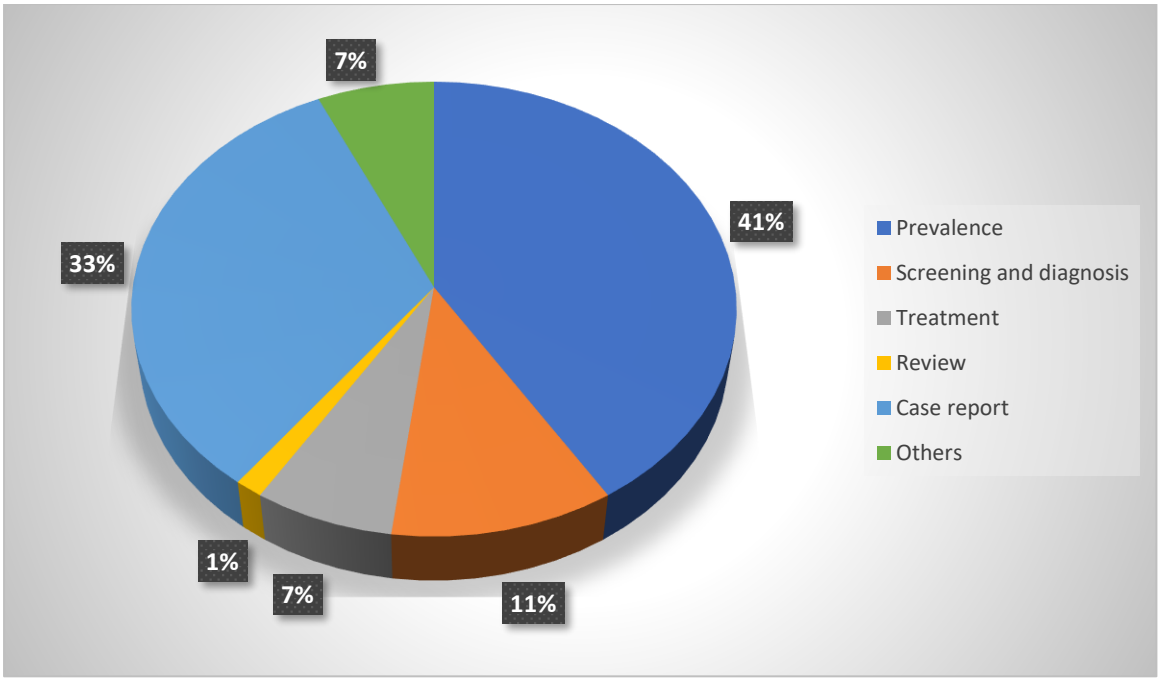
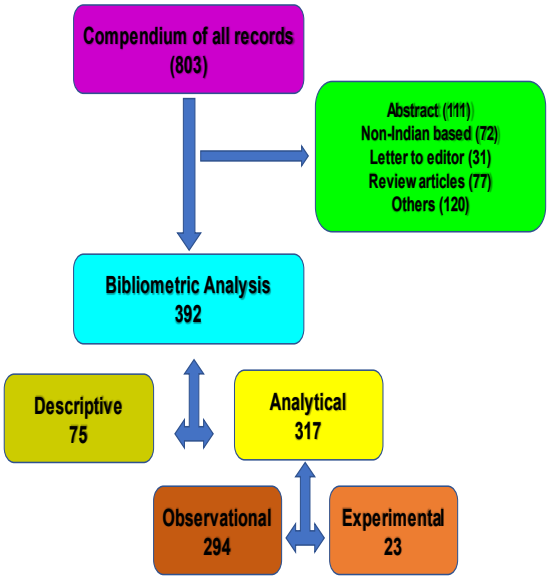


Figure 2- Thematic distribution of studies conducted in Odisha

Over the past five decades, there has been remarkable progress in the field of sickle cell disease research in India not only to analyze its determinants, rather find out the effective and cost-effective means for diagnosis and management of such life-threatening conditions. However, as more data and pieces of evidence are evolved dramatically, it is cumbersome to understand how, when and why to translate these researches into practice. The compendium summarizes key information regarding disease burden, its determinants and detrimental consequences, proven therapies and evidence-based health care such as newborn screening, health education, prophylaxis for education, optimal nutrition and hydration, blood transfusion, hydroxyurea therapy etc. for reduction of sickle cell-related adverse effects (e.g., pain crisis, acute chest syndrome, hospitalization, mortality and so on), which will help different national and subnational stakeholders to make the best use of the available evidence for designing and implementing an acceptable, affordable, appropriate and sustainable policy and program to prevent and control SCD. In addition, such compendium plays a vital role in drawing the portrait of sickle cell disease research to analyze the research trend, actors, focus and funding sources through bibliometric analysis. Furthermore, this compendium of evidence will be beneficial for researchers to identify several gaps that need further attention for improvising the understanding of biological as well as the social aspect of such incurable disease in a middle-income country like India.

Bibliometric analysis- Key findings



The majority of primary (as well as corresponding) authors were from these states leading research on SCD in India with Maharashtra (100) followed by Odisha (54) and New Delhi (44) leading the list.

While 22.7% of the studies were exclusively among children, 25.5% were in adult participants

12.24% (48) studies on SCD were carried out exclusively among Tribal populations with a majority of these from the state of Odisha

- **<u>Important deliverables:</u>**

  A manuscript titled "Research on Sickle cell disease in India- a bibliometric analysis over 7 decades" was submitted to the Indian Journal of Medical Research on November 30, 2021.

SECTION-2

Objective

GIS Mapping of the Sickle Cell Anaemia Pockets in the TSP Areas.

Summary

Scheduled Tribes (STs) constitute around 8% of the population in India and are generally residents in well-recognized pockets. Odisha is unique among Indian states in that it has a large (22.85% of ST population) and diverse (62 Scheduled Tribes and 13 Particularly Vulnerable Tribal Groups (PVTGs)) tribal population. To protect their interest and preserve their culture along with the development process, special provisions have been made to give special treatment to these tribal people and these areas are known as the Tribal Sub-plan Areas (TSP). In Odisha out of 30 districts, 13 districts which comprise a sizeable population of tribal inhabitants are covered under the TSP areas.

Methodology

The information regarding the sickle cell cases was collected for the 13 districts of Odisha. The data were collected for sickle cell cases including Sickle cell disease and sickle cell trait. The GIS map was generated using QGIS software (Open source) version 3.20. State, district and block level maps were prepared. Interactive GIS maps were also created using the same software.

Key Findings

Sl no	District	Sickle cell disease	Sickle cell trait	Total
1	Balasore	2	2	4
2	Mayurbhanja	45	59	104
3	Keonjhar	215	264	479
4	Sambalpur	577	784	1361
5	Sundargarh	1426	1581	3007
6	Deogarh	282	425	707

7	Gajapati	37	67	104
8	Kalahandi	90	174	264
9	Rayagada	200	328	528
10	Koraput	423	739	1162
11	Malakangiri	12	14	26
12	Nowrangapur	78	134	212
13	Kandhamal	903	1206	2109
	Total	4290	5777	10067

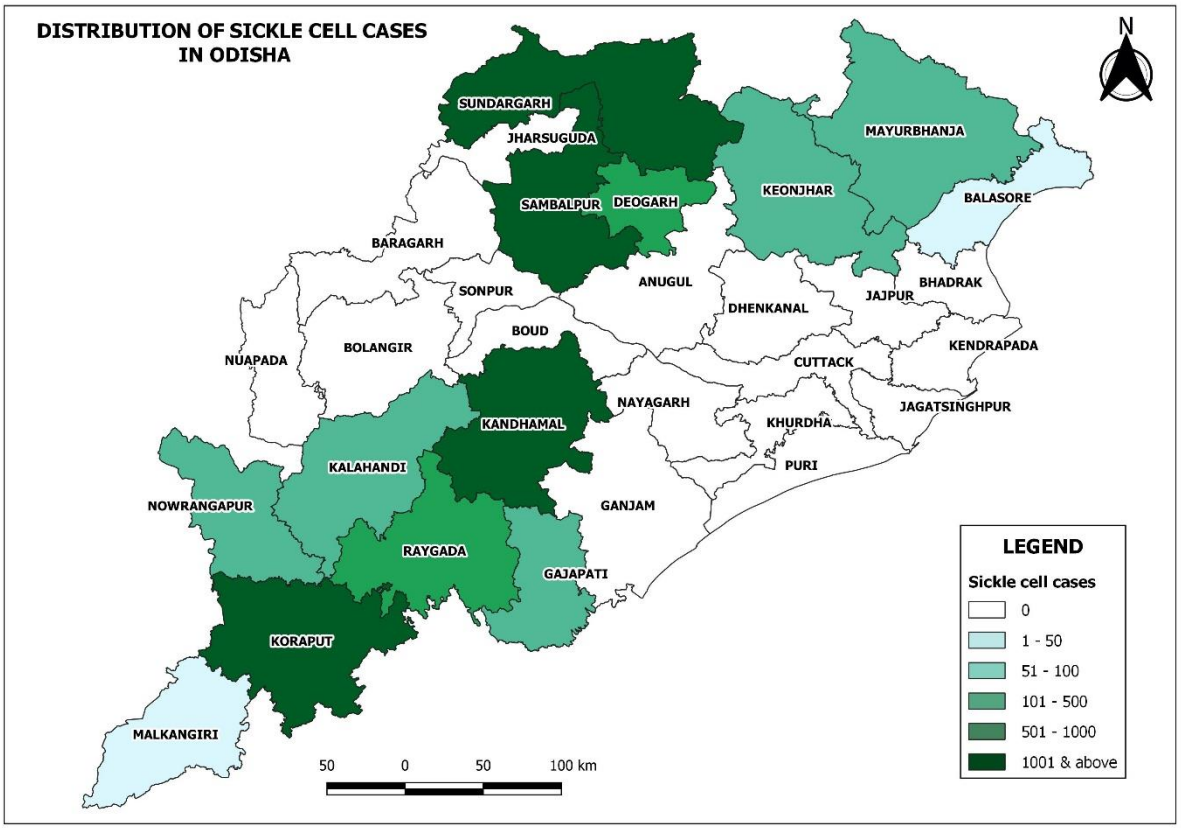


Figure 3- Distribution of Sickle cell cases in Odisha

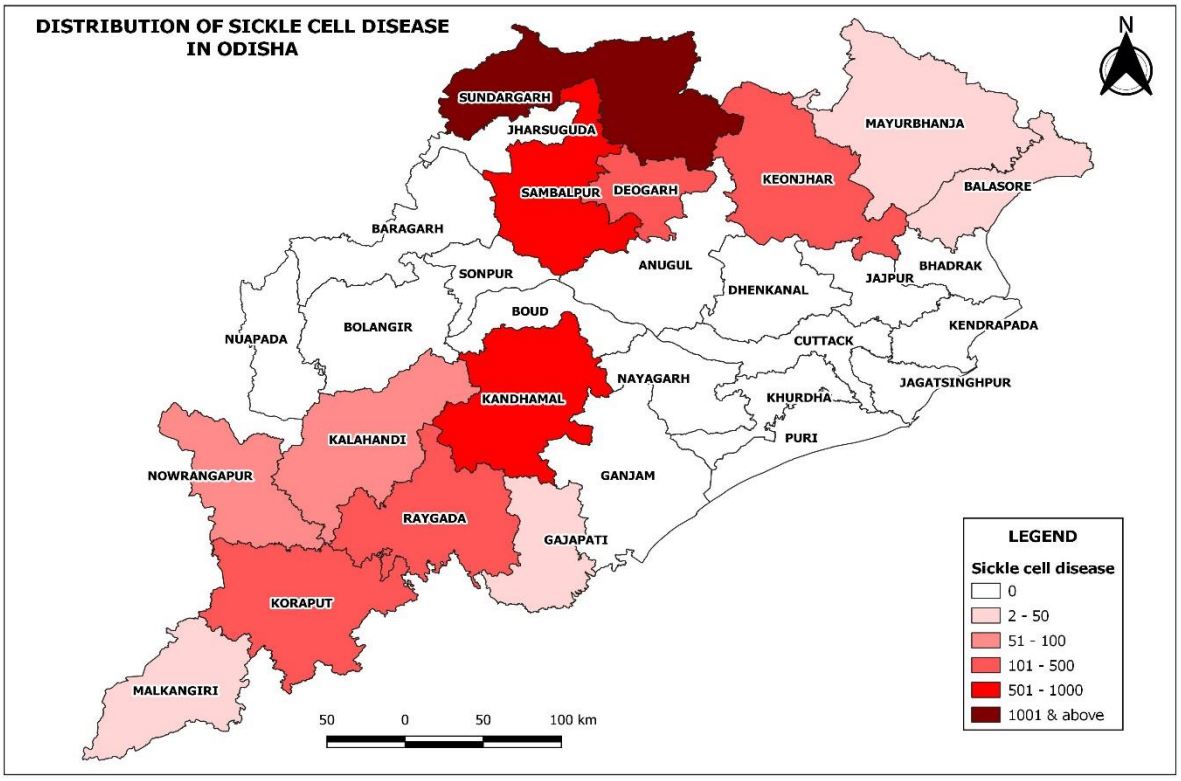


Figure 4- Distribution of Sickle cell disease in Odisha

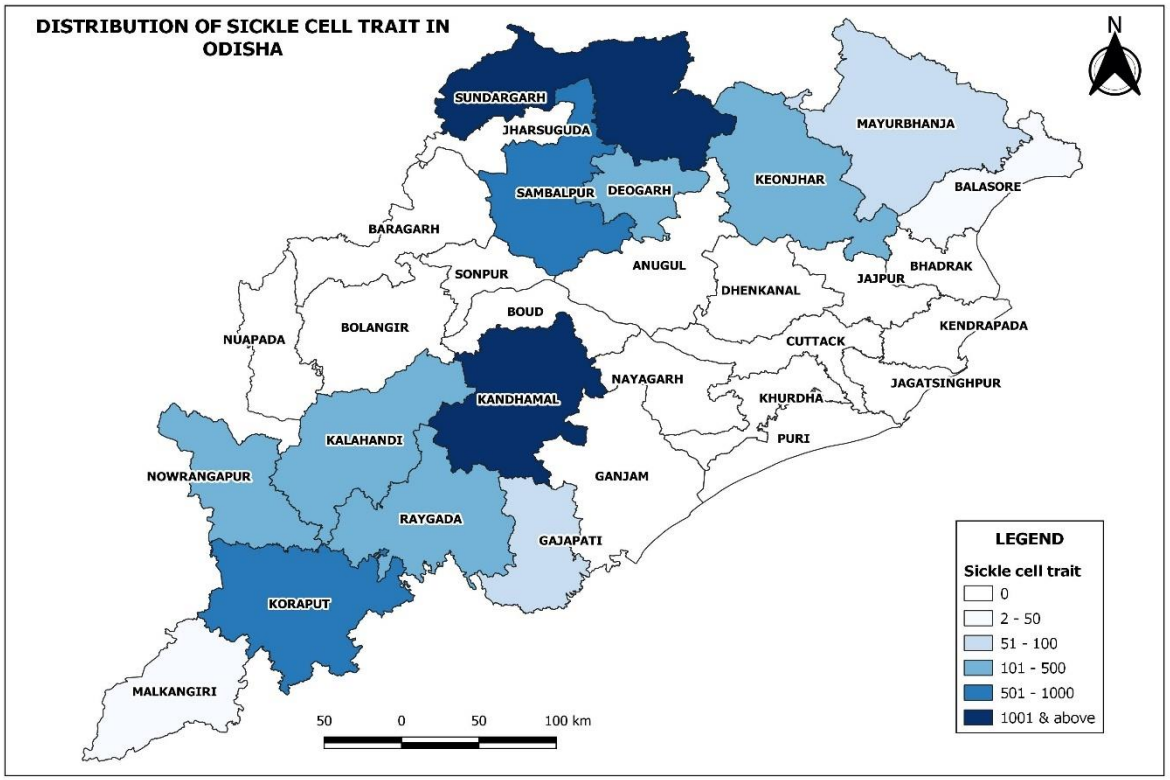


Figure 5- Distribution of Sickle cell trait in Odisha

SECTION-3

Objective

Building and piloting for feasibility of implementation of a minimum dataset and associated android applications necessary to prepare a prospective registry of sickle cell anaemia patients in Odisha belonging to tribal communities (Development of a Portal and application development to capture data pertaining to sickle cell anaemia patients from tribal communities).

Summary

The support corner was envisioned as a one-stop portal with information about SCD in Tribal Regions of India. The portal gives access to real-time data to every visitor through a dashboard, and online self-registration facility, and acts as a knowledge repository with information about the disease and various government initiatives. The Ministry of Tribal Affairs, Govt. of India, has built and recently made available a similar portal with the same goals. Therefore, as per the discussion with team at SCSTRTI, as there was one existing portal it was decided to carry out a qualitative review to access the usability and feasibility of the Sickle Cell Corner Portal and provide suggestions to improve it by piloting in the field.

Methodology

A qualitative review for assessing the feasibility, usability and acceptability of the Sickle Cell Corner Portal in the Kandhamal district was carried out in the first week of January 2022.

The study was aimed to qualitatively examine the feasibility, usability, and acceptability of the Sickle Cell Corner Portal.

The qualitative study was carried out among key stakeholders Doctors, Programme Managers and community health workers using In-depth and key-informant interviews.

Key findings

- Majority of the Study participants were not aware of the portal.
- All pointed out that the portal is a good initiative, but patients will not register if there is no financial benefit.
- Most tribal people, being deprived of basic education and a cell phone will not be able to use the portal.

- In villages network issue is there, so assessing the portal is difficult.
- The material in the portal is in the English language and most of the patients are illiterates.

Way forward

- ASHAs and ANMs can be trained for uploading data of sickle cell patients in the portal.
- The portal can be a part of any government program which will help in making it mandatory.
- The portal can be linked with the disability certificate or blood bank where data can be collected at a single point.

❖ **Important deliverables:**

Due to the availability of a Govt. portal during the study conduct, it was mutually decided to avoid redundancy by working on the existing portal and pilot it for feasibility in tribal and remote communities.

GIS MAPPING-SICKLE CELL POCKETS IN TSP AREAS

ODISHA

Odisha

Sl no	District	Sickle cell diseases	Sickle cell trait	Total
1	Balasore	2	2	4
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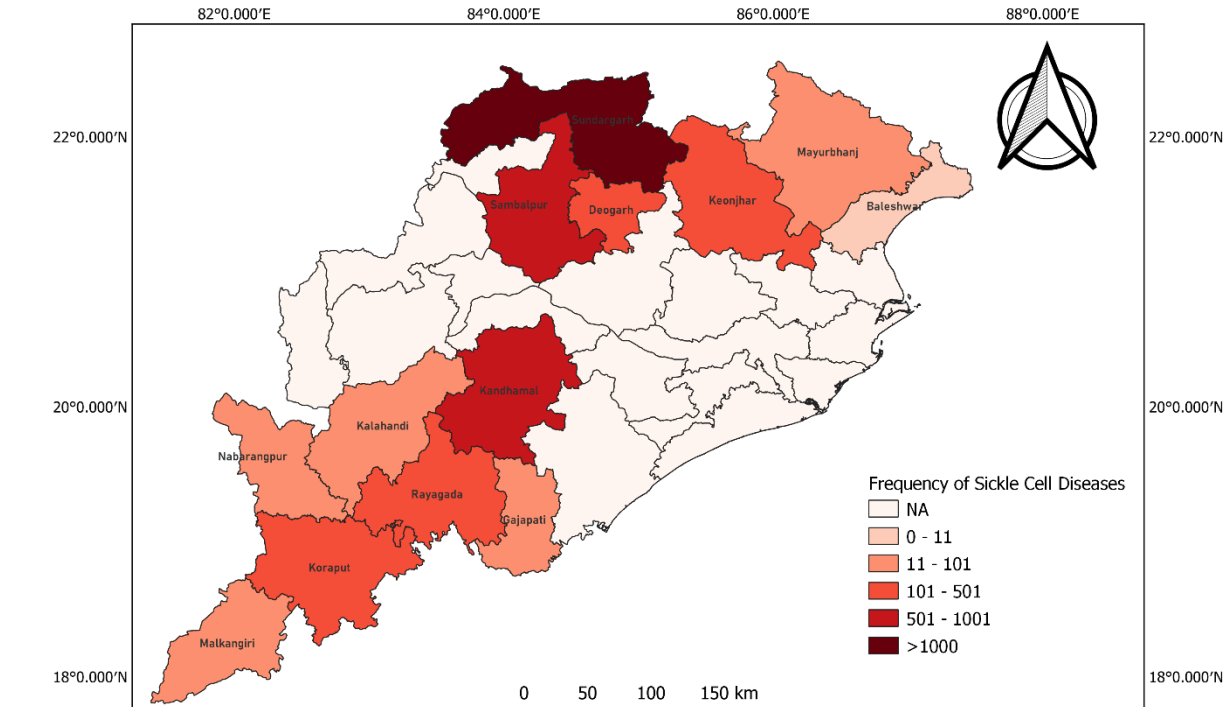

Figure 1 Prevalence of Sickle cell disease

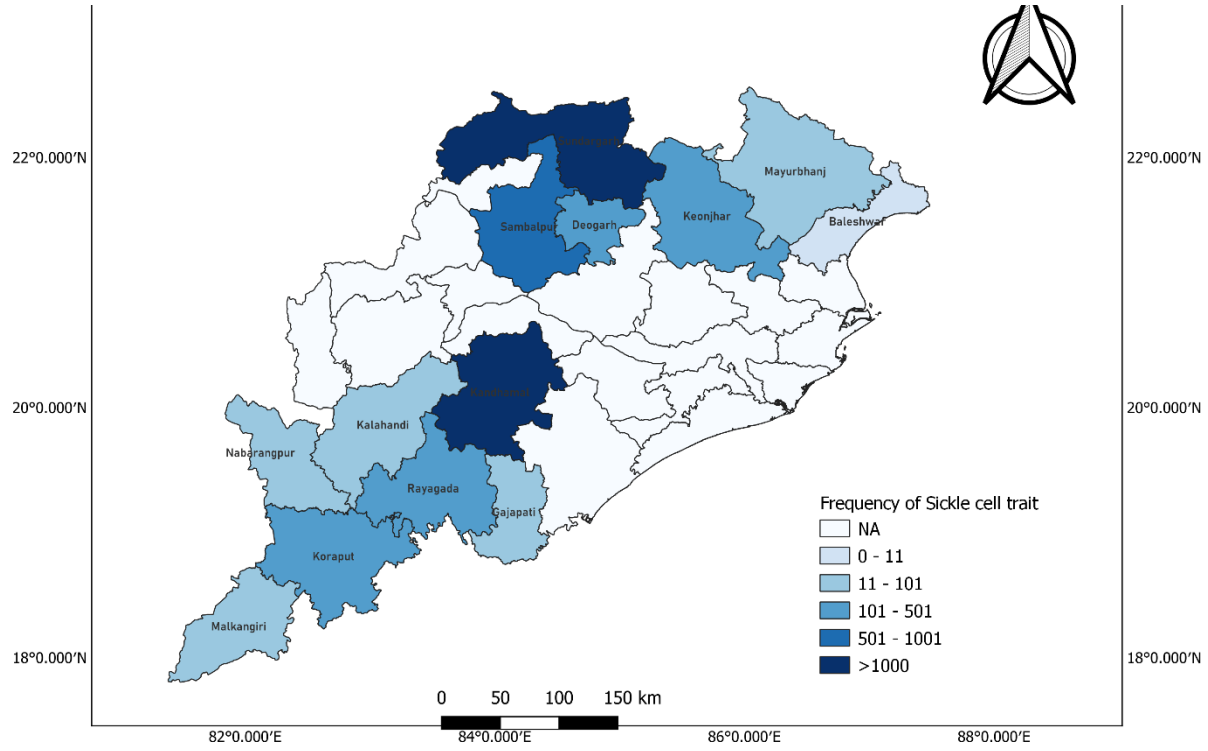

Figure 2 Prevalence of Sickle cell trait

Balasore

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Balasore	Nilagiri	2	2	4
Total		2	2	4

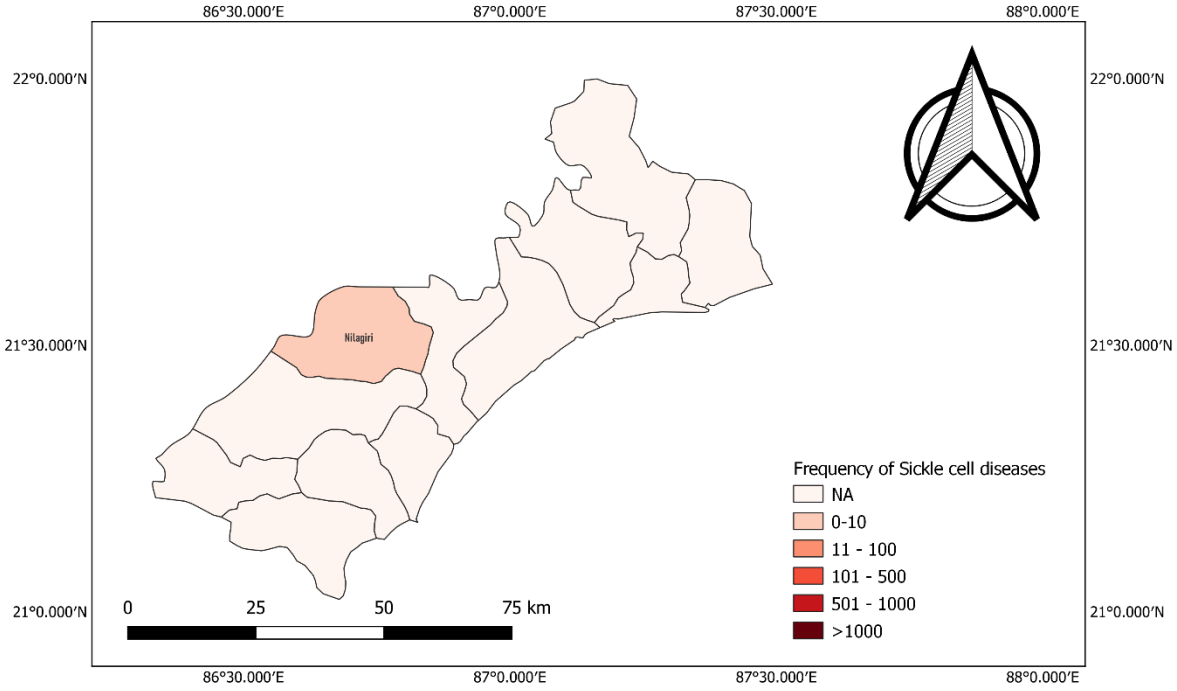

Figure 3 Prevalence of Sickle cell disease- Balasore

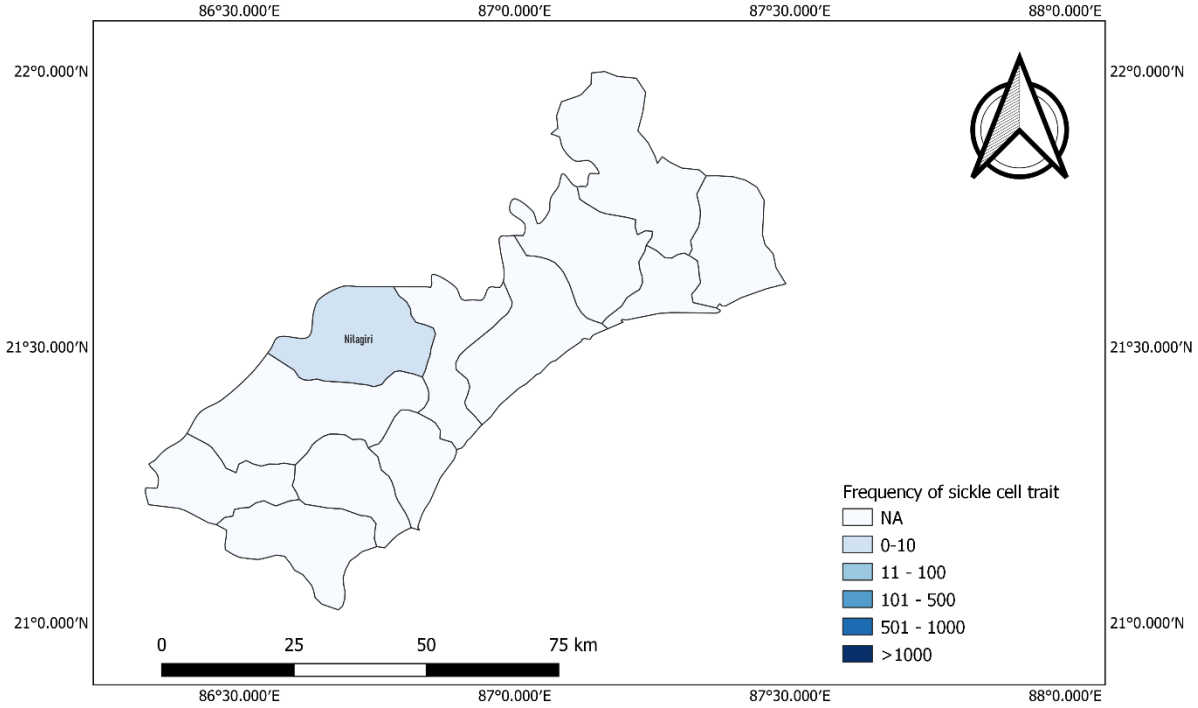

Figure 4 Prevalence of Sickle cell trait- Balasore

Mayurbhanj

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Mayurbhanj	Baripada	5	7	12
	Badasahi	0	1	1
	Samakhunta	Not Available	Not Available	Not Available
	Betanati	1	0	1
	Rasgovindpur	Not Available	Not Available	Not Available
	Muruda	Not Available	Not Available	Not Available
	Bangiriposi	Not Available	Not Available	Not Available
	Saraskana	Not Available	Not Available	Not Available
	Kuliana	Not Available	Not Available	Not Available
	Suliapada	0	2	2
	Khunta	2	2	4
	Gopubandhunagar	Not Available	Not Available	Not Available
	Kaptipada	Not Available	Not Available	Not Available
	Udala	2	3	5
	Karanjia	6	7	Not Available
	Raruan	7	6	13
	Joshipur	5	8	13
	Thakurmunda	5	9	14
	Sukruli	7	7	14
	Bisoi	1	1	2
	Bijatola	1	2	3
	Kusumi	Not Available	Not Available	Not Available
	Rairangapur	2	1	3
	Tiring	Not Available	Not Available	Not Available
	Bahalda	1	3	4
	Jamda	Not Available	Not Available	Not Available
Total		45	59	104

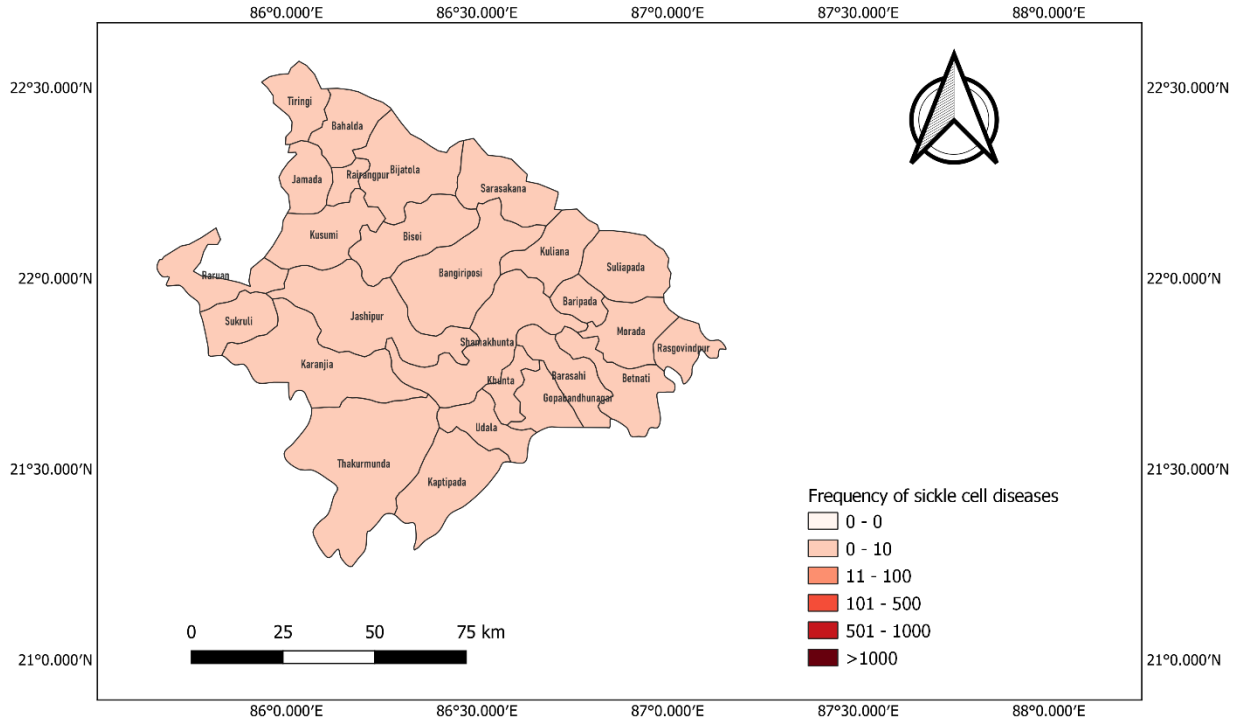

Figure 5 Prevalence of Sickle cell disease- Mayurbhanj

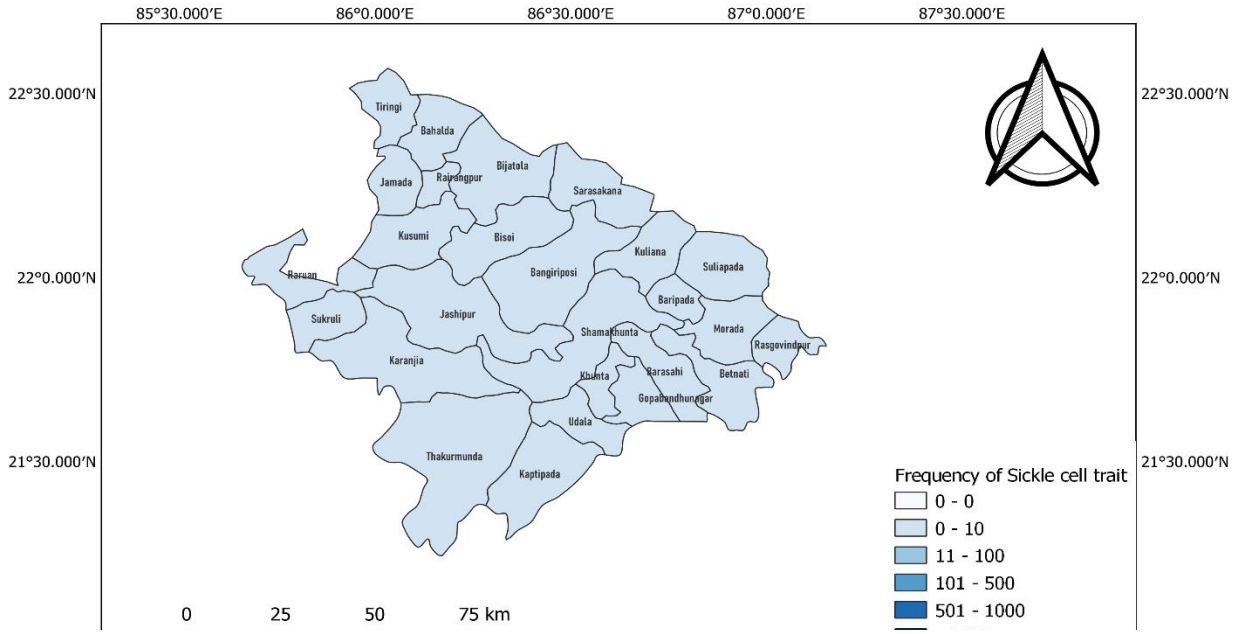

Figure 6 Prevalence of Sickle cell trait- Mayurbhanj

Keonjhar

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Keonjhar	Joda	8	18	26
	Champua	14	19	33
	Jhumpura	6	10	16
	Patna	8	10	18
	Ghatgaon	3	4	7
	Keonjhar	41	55	96
	Saharpada	5	3	8
	Harichandanpur	25	21	46
	Telkoi	101	106	207
	Bansapal	4	18	22
Total		215	264	479

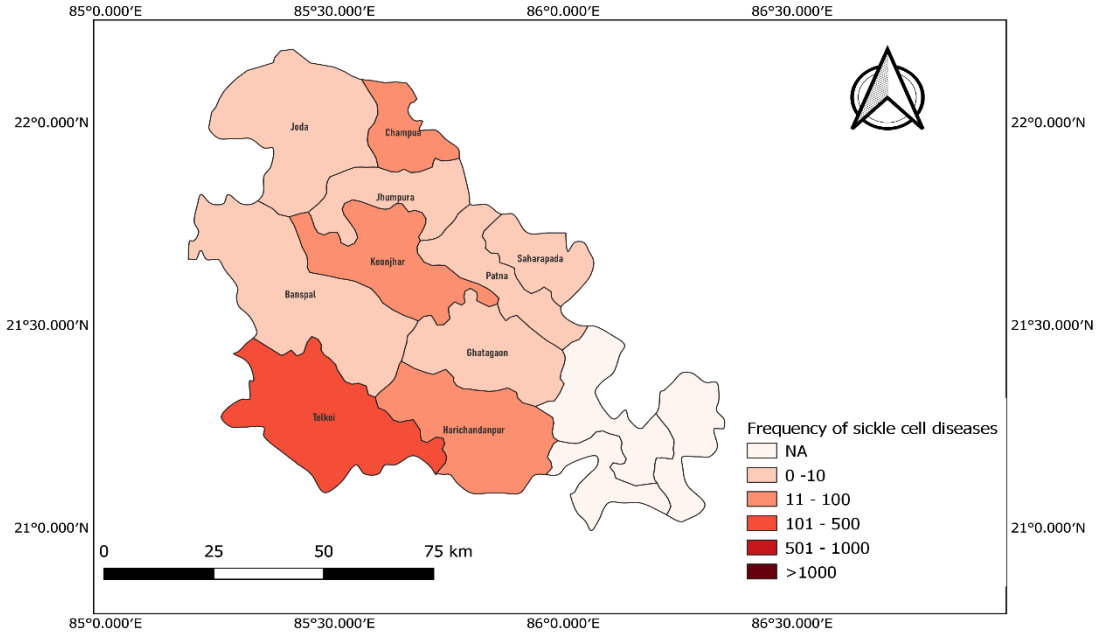

Figure 7 Prevalence of Sickle cell disease- Keonjhar

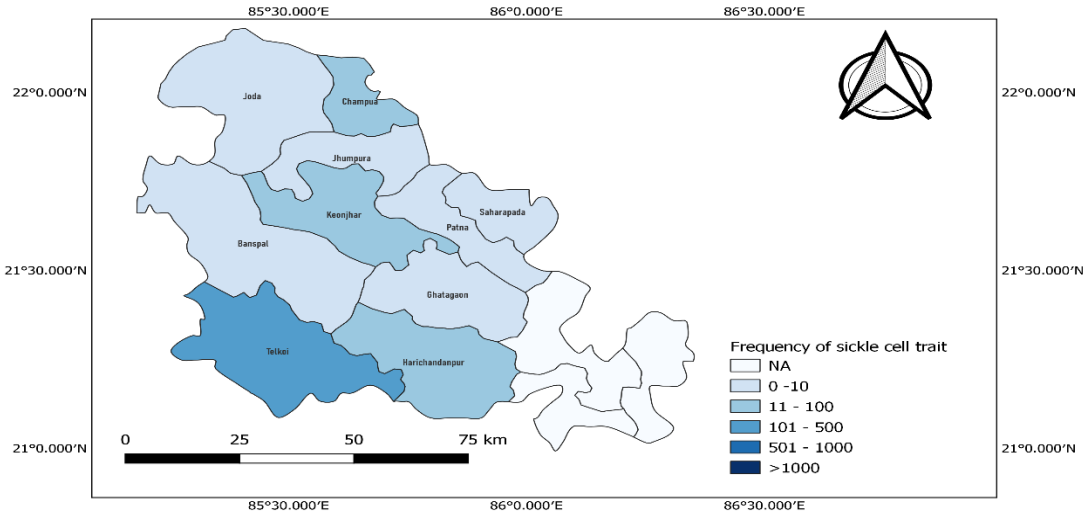

Figure 8 Prevalence of Sickle cell trait- Keonjhar

Sambalpur

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Sambalpur	Kuchinda	196	298	494
	Bamra	169	188	357
	Jamankira	212	298	510
Total		577	784	1361

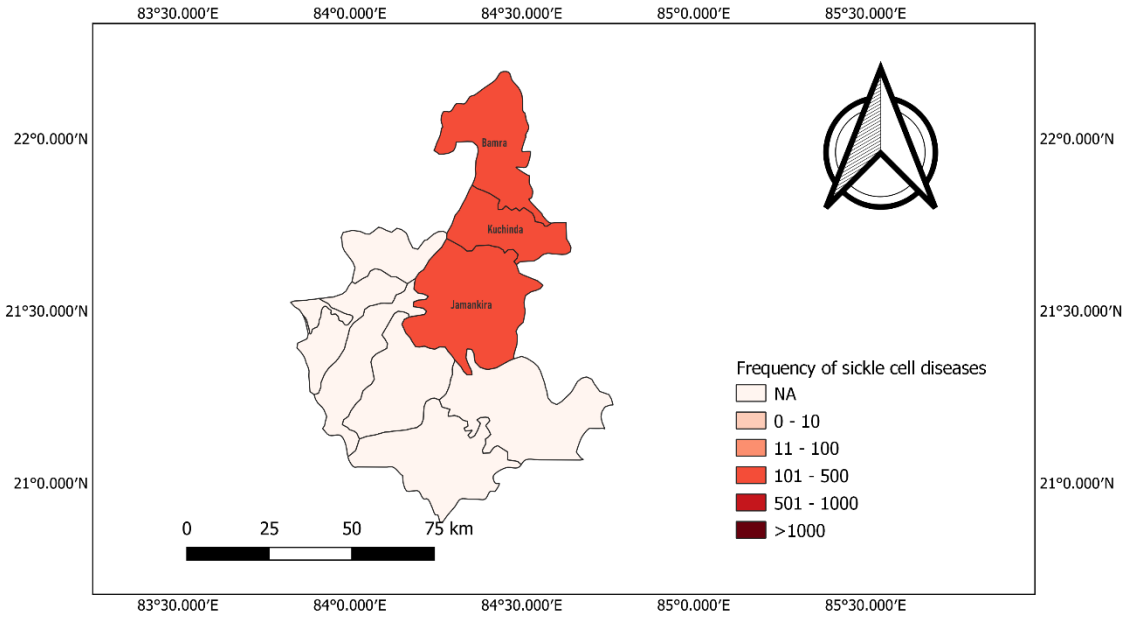

Figure 9 Prevalence of Sickle cell disease- Sambalpur

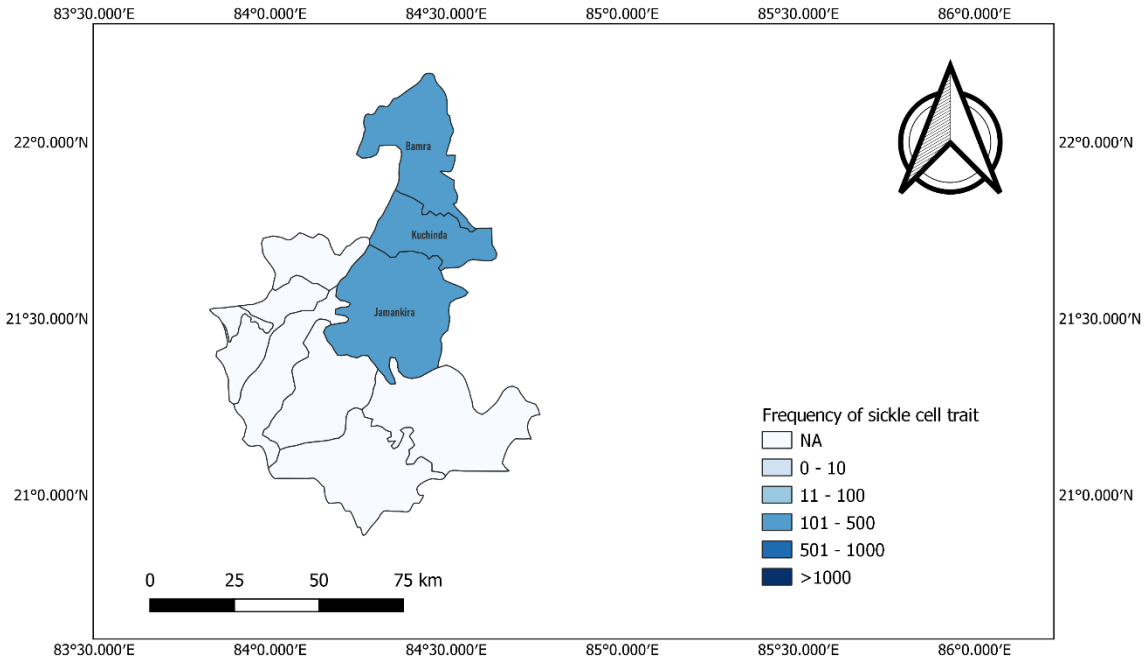

Figure 10 Prevalence of Sickle cell trait- Sambalpur

Sundergarh

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Sundergarh	Bonaigarh	68	88	156
	Lahunipara	27	25	52
	Gurundia	17	16	33
	Koida	1	2	3
	Kuarmunda	30	20	50
	Bisra	27	22	49
	Nuagaon	17	21	38
	Lathikata	88	94	182
	Sundergarh	431	509	940
	Subdega	60	62	122
	Ballisankara	83	89	172
	Lephripara	158	192	350
	Badagaon	107	112	219
	Tangarpalli	105	109	214
	Hemgir	126	145	271
	Kutra	35	39	74
	Rajagangpur	46	36	82
Total		1426	1581	3007

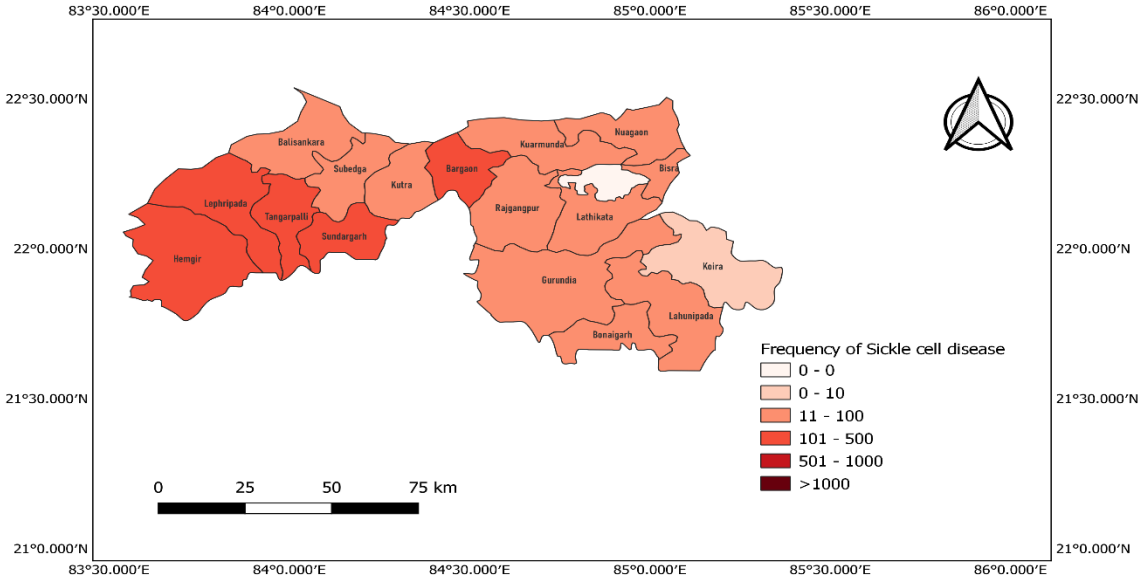

Figure 11 Prevalence of Sickle cell disease- Sundergarh

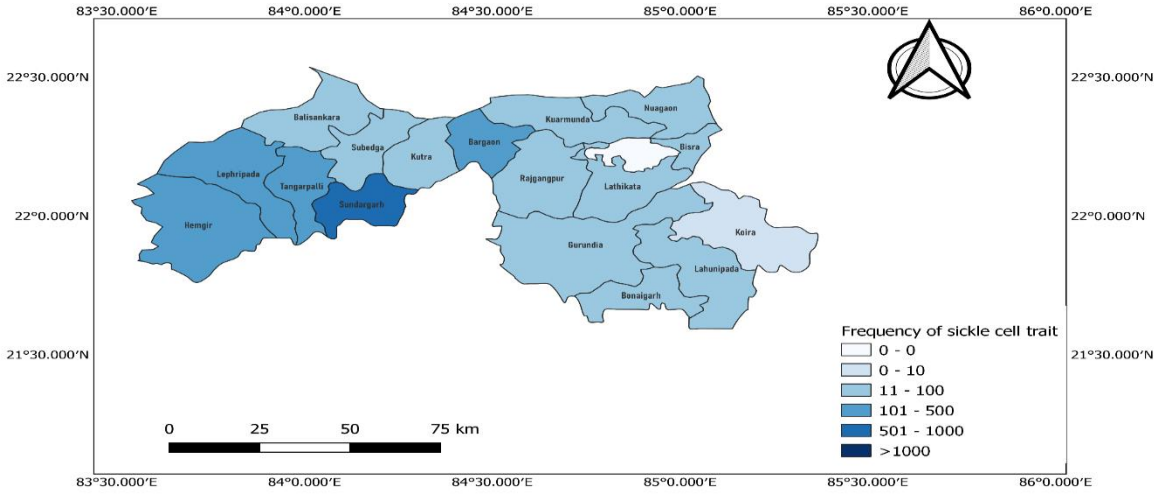

Figure 12 Prevalence of Sickle cell trait - Sundergarh

Deogarh

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Deogarh	Teleibani	282	425	707
Total		282	425	707

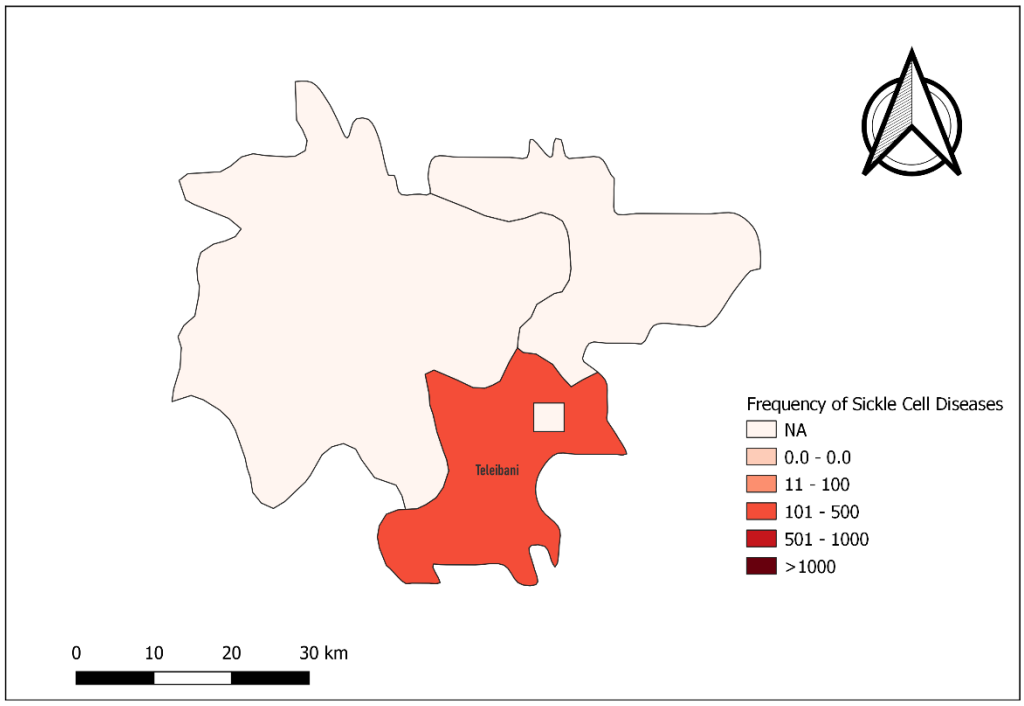

Figure 13 Prevalence of Sickle cell disease- Deogarh

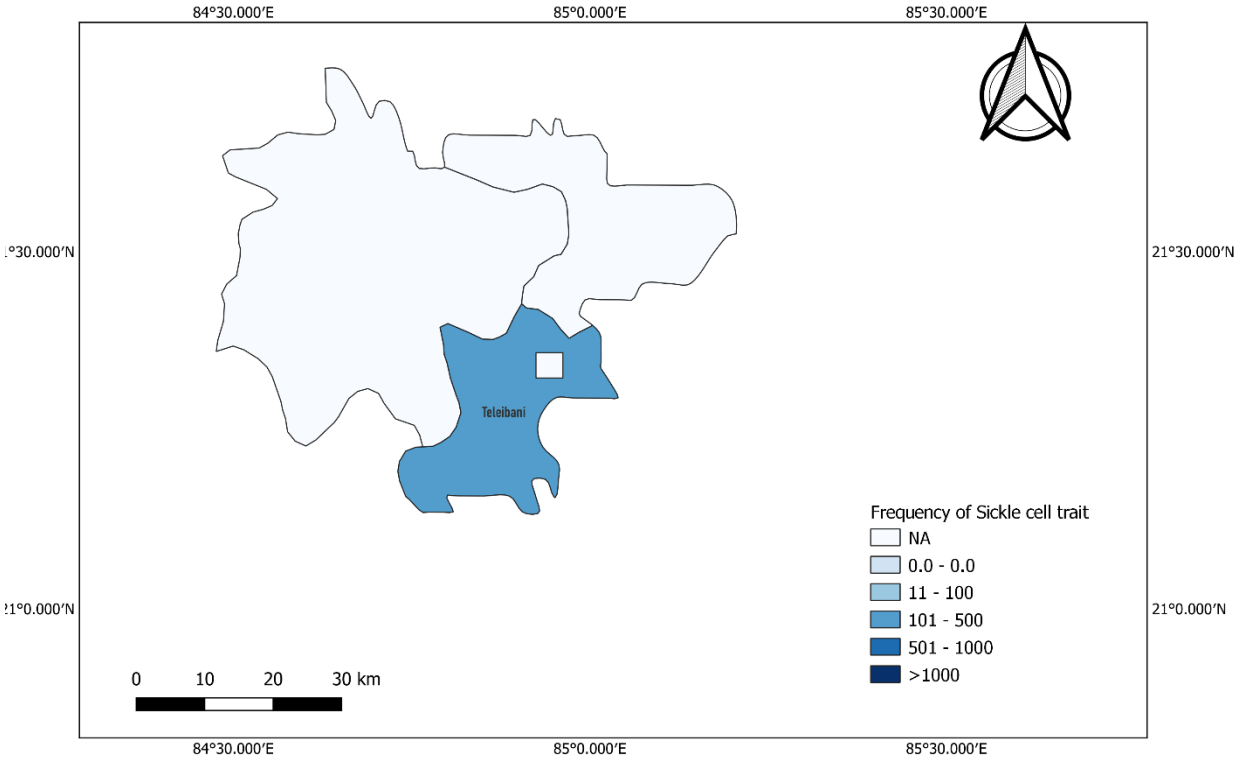

Figure 14 Prevalence of Sickle cell trait - Deogarh

Gajapati

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Gajapati	Guma	15	23	38
	Rayagada	13	23	36
	Mohana	6	10	16
	R Udayagiri	2	8	10
	Nuagada	1	3	4
Total		37	67	104

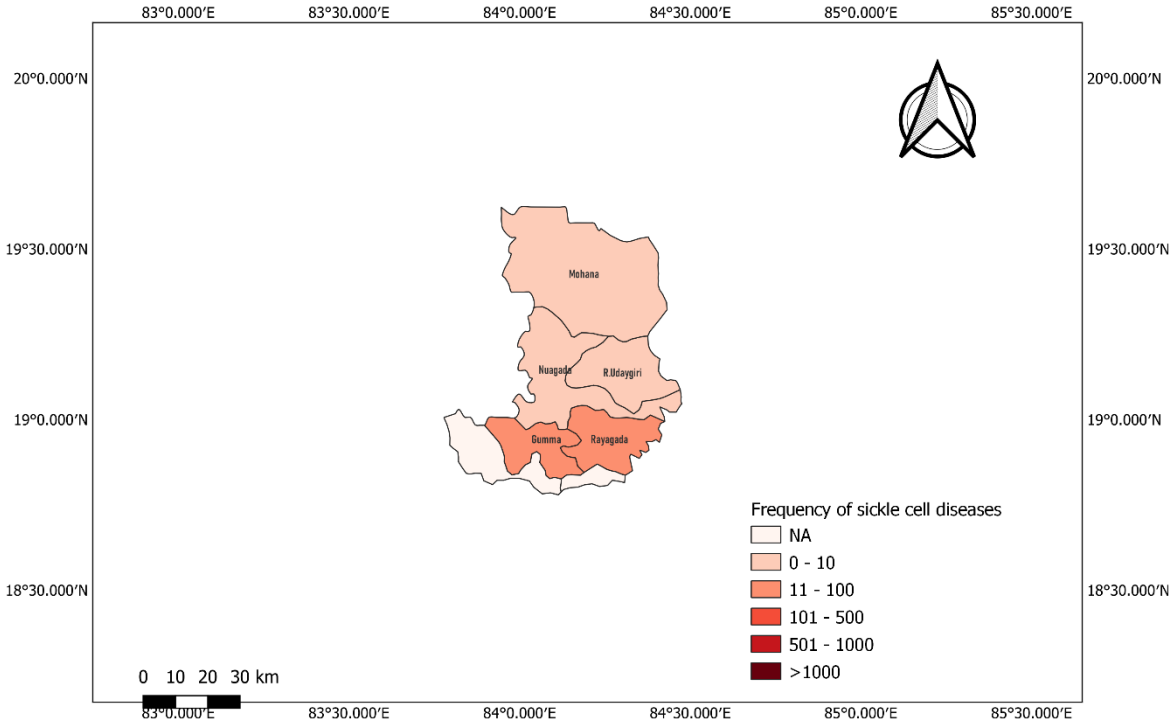

Figure 13 Prevalence of sickle cell disease- Gajapati

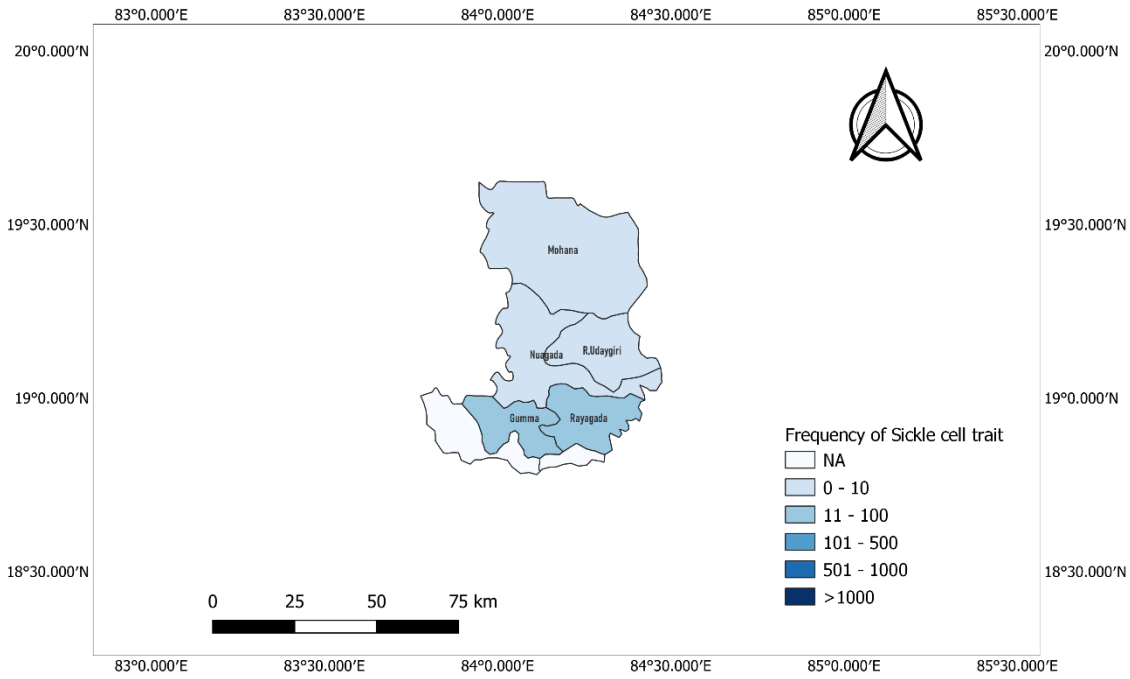

Figure 16 Prevalence of Sickle cell trait - Gajapati

Kalahandi

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Kalahandi	Th Rampur	16	22	38
	Lanjigarh	68	68	136
Total		84	90	174

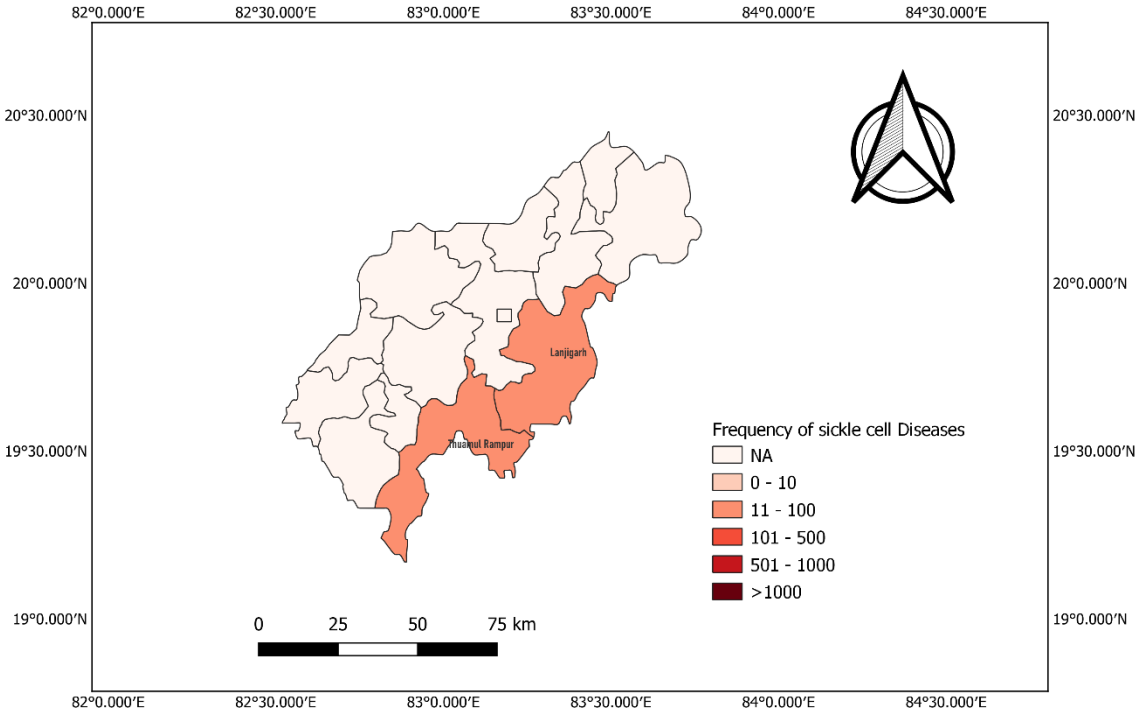

Figure 17 Prevalence of Sickle cell disease - Kalahandi

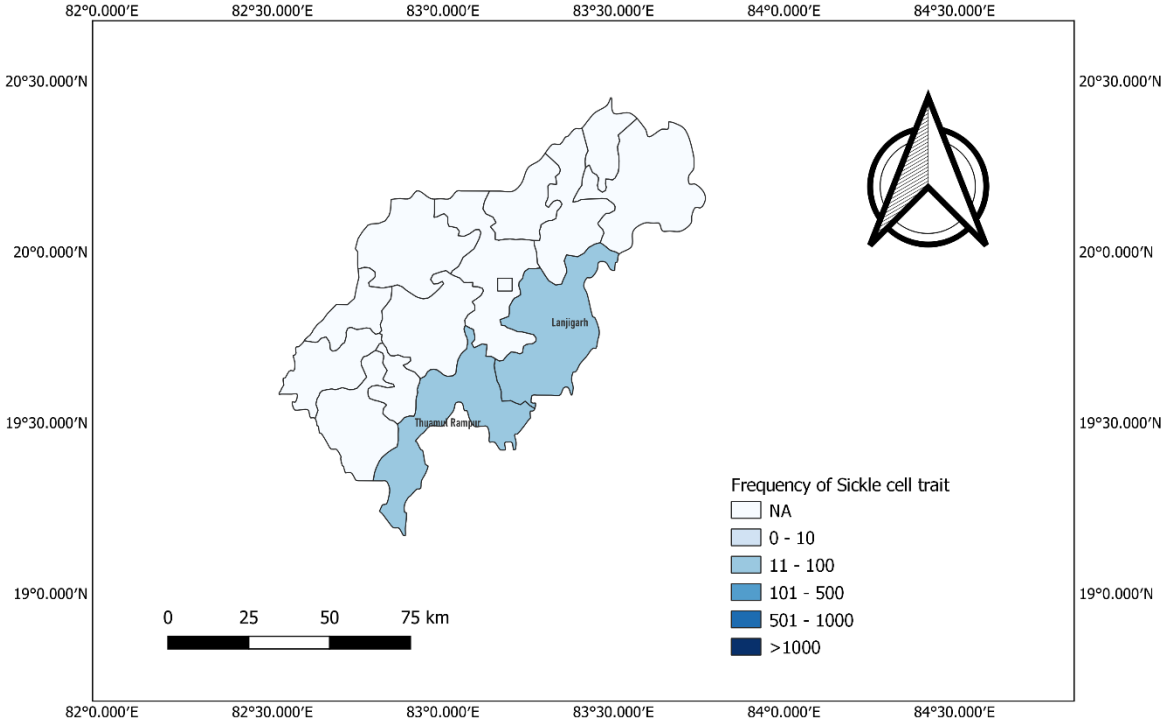

Figure 18 Prevalence of Sickle cell trait - Kalahandi

Rayagada

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Rayagada	Gunupur	12	20	32
	Gudari	3	5	8
	Padmapur	4	12	16
	Ramnaguda	5	13	18
	Bishamakatak	21	29	50
	Muniguda	43	56	99
	Chandrapur	1	1	2
	Rayagada	43	72	115
	Kolnara	9	13	22
	Kashipur	52	85	137
	Kalyansinghpur	7	22	29
Total		200	328	528

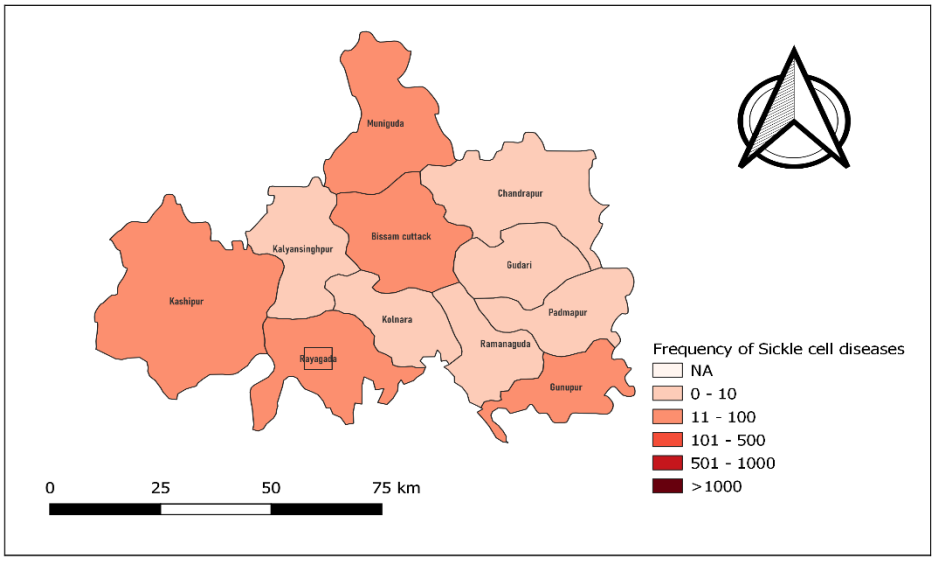

Figure 19 Prevalence of Sickle cell disease - Rayagada

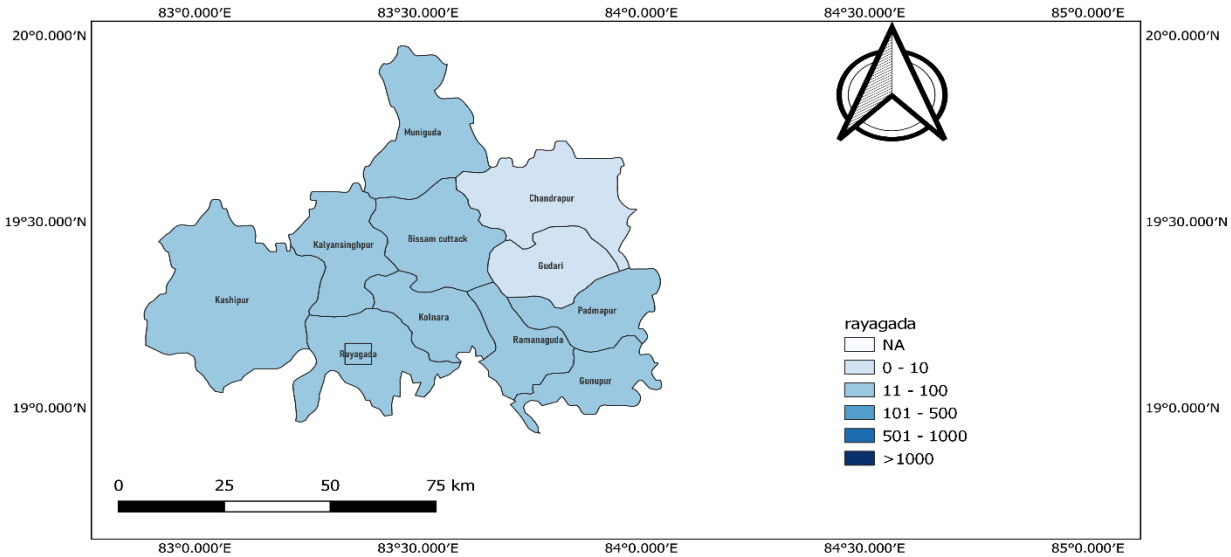

Figure 20 Prevalence of Sickle cell trait - Rayagada

Koraput

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Koraput	Jeypore	33	40	73
	Boriguma	23	23	46
	Kotpad	5	4	9
	Boipariguda	17	18	35
	Kundra	11	12	23
	Koraput	86	135	221
	Similiguda	23	26	49
	Pottangi	9	8	17
	Nandapur	12	15	27
	Dasmanthpur	12	16	28
	Lamtapur	20	19	39
	Narayanpatna	12	16	28
	Laxmipur	43	69	112
	Bandhugaon	10	22	32
Total		316	423	739

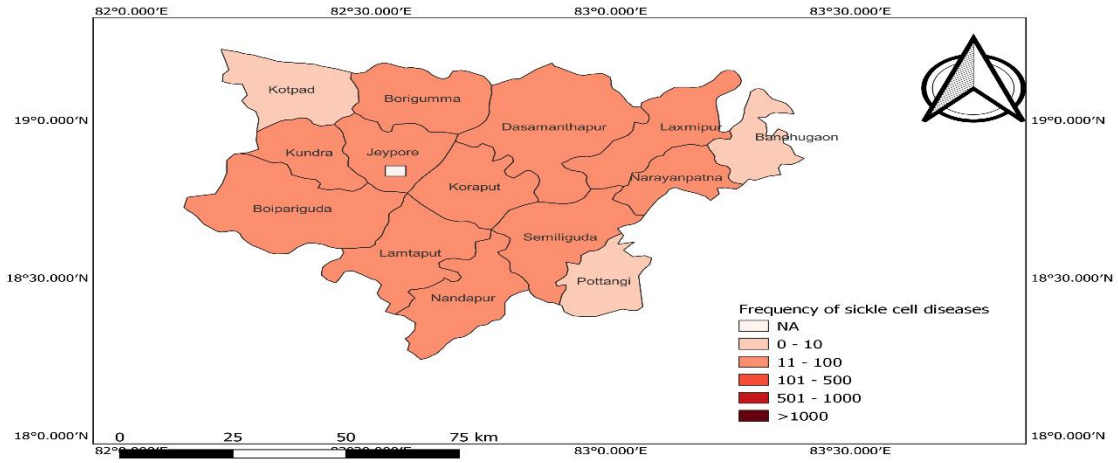

Figure 21 Prevalence of Sickle cell disease - Koraput

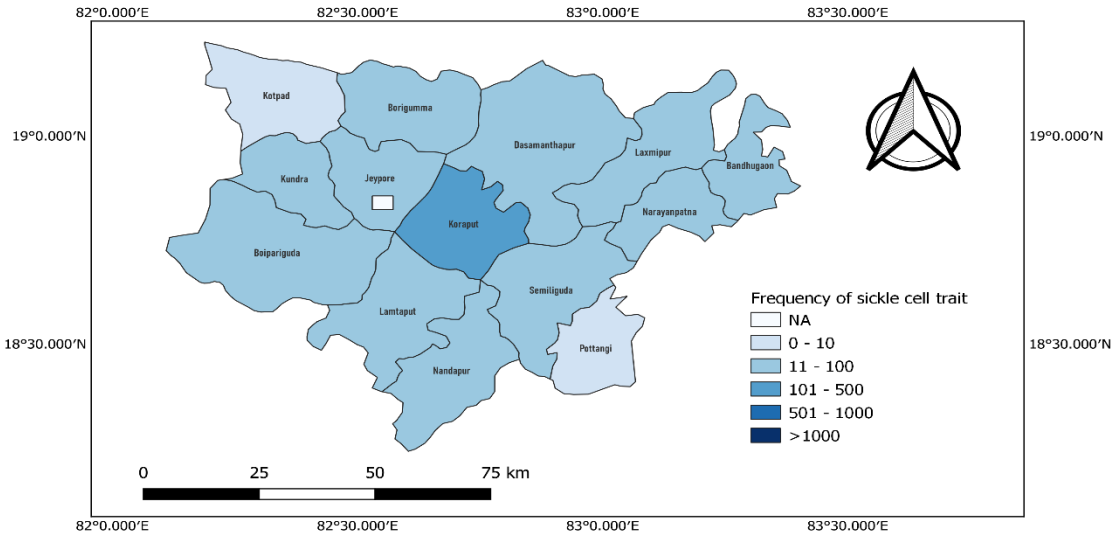

Figure 22 Prevalence of Sickle cell trait - Koraput

Malkangiri

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Malkanagiri	Malkanagiri	6	3	9
	Korkunda	4	6	10
	Kalimela	Not Available	Not Available	
	Podia	0	2	2
	Khirput	1	2	3
	Kuduluguma	Not Available	Not Available	Not Available
	Mathili	1	1	2

Total		12	14	26

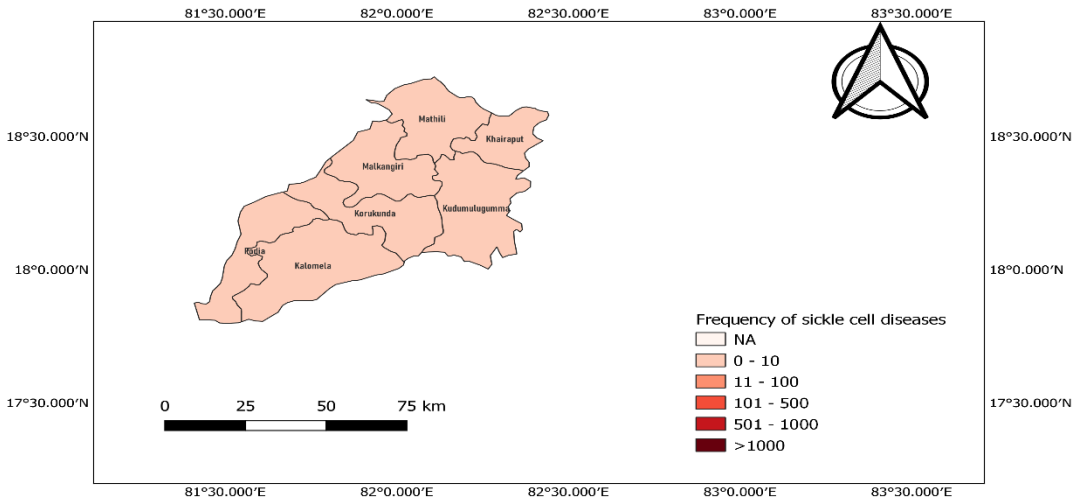

Figure 23 Prevalence of Sickle cell disease - Malkangiri

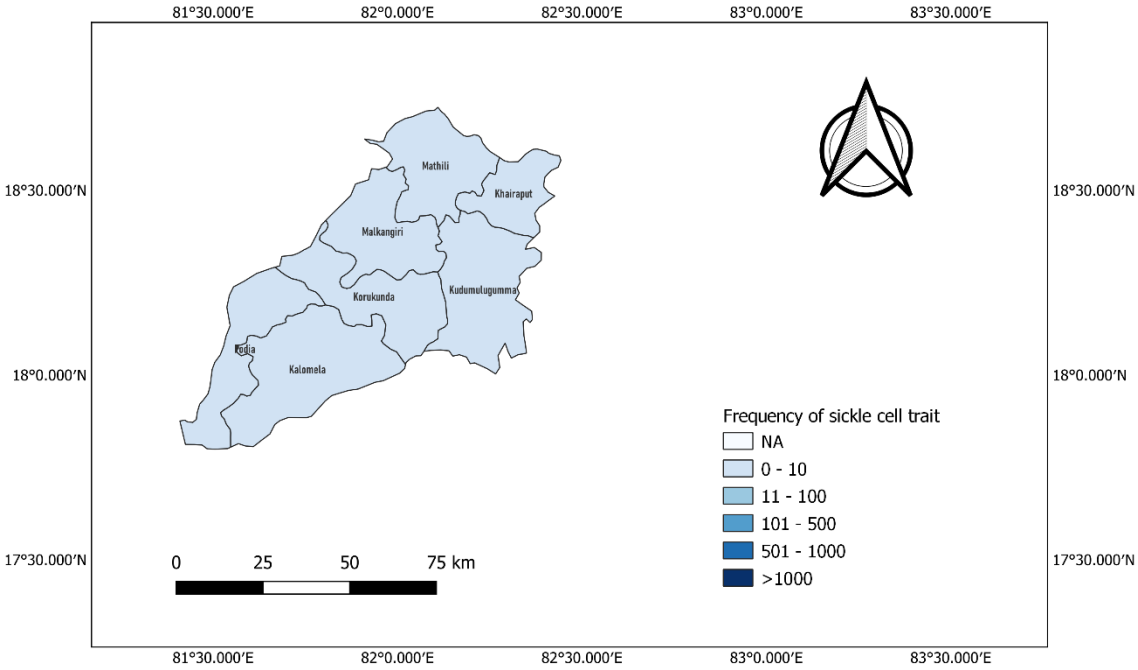

Figure 24 Prevalence of Sickle cell trait - Malkangiri

Nowrangapur

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Nowrangapur	Nowrangpur	10	21	31
	Tentulikhunti	23	27	50
	Papadahandi	5	9	14
	Nandanhandi	4	5	9
	Kosagumunda	5	7	12
	Raighra	0	4	4
	Umerkote	2	0	2
	Chandanhandi	2	0	2
	Jharigaon	Not Available	Not Available	Not Available
	Dabugaon	5	5	10
Total		56	78	134

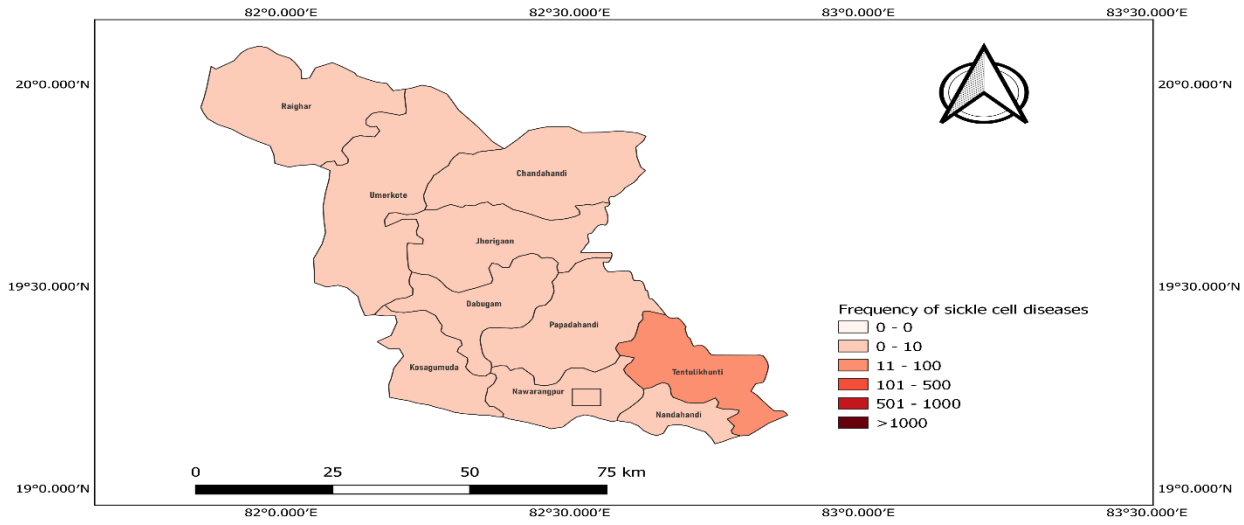

Figure 25 Prevalence of Sickle cell disease - Nowrangapur

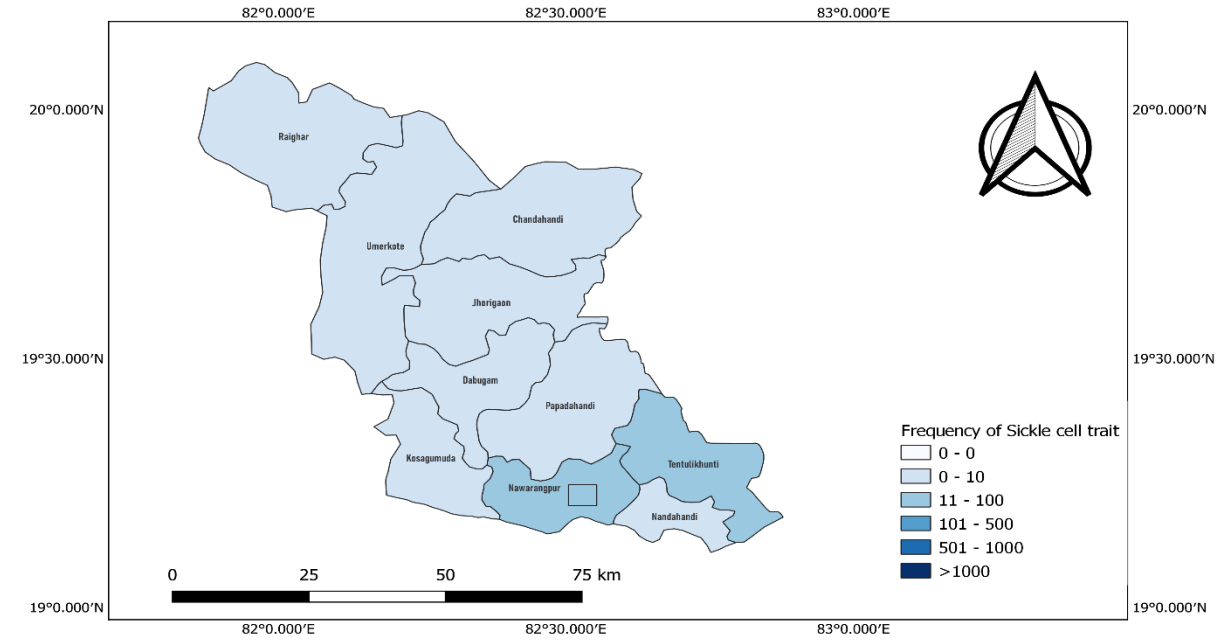

Figure 26 Prevalence of Sickle cell trait - Nowrangapur

Kandhamal

District	TSP Blocks	Sickle cell diseases	Sickle cell trait	Total
Kandhamal	Baliguda	89	110	199
	K Nuagaon	75	72	147
	Daringibadi	65	85	150
	Tumudibandha	63	154	217
	Kotagarh	37	57	94
	Tikabali	76	83	159
	G. Udagiri	58	76	134
	Raikia	47	42	89
	Chakapada	48	61	109
	Phulbani	139	198	337
	Phiringia	90	132	222
	Khajuripada	116	136	252
Total		903	1206	2109

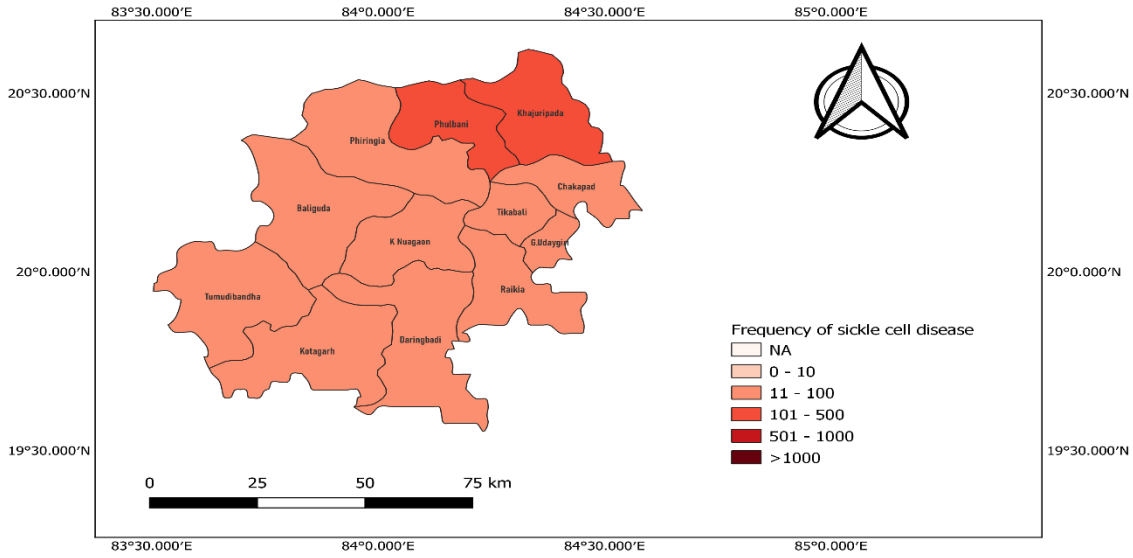

Figure 27 Prevalence of Sickle cell diseaset - Kandhamal

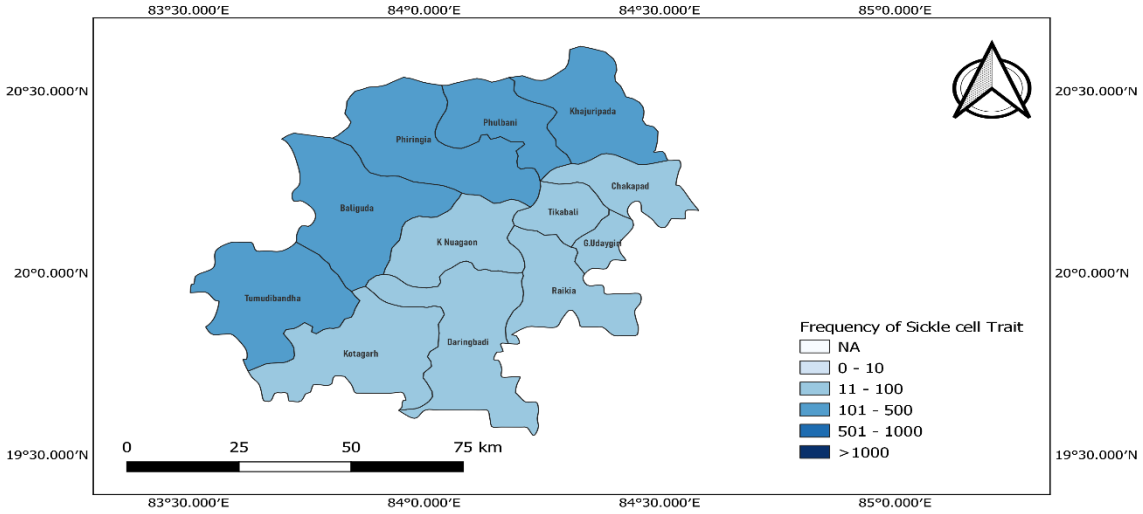

Figure 28 Prevalence of Sickle cell trait - Kandhamal

Ministry of Tribal Affairs,
Government of India

icmr INDIAN COUNCIL OF MEDICAL RESEARCH | RMRCBB REGIONAL MEDICAL RESEARCH CENTRE, BHUBANESWAR

SCSTRTI
ST & SC Development, Minorities & Backward Classes Welfare Department, Govt. of Odisha.

Compendium on Evidence Based Researches on SICKLE CELL ANAEMIA IN INDIA

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Compendium

on

Evidence Based Researches

On

SICKLE CELL ANAEMIA IN INDIA

A Joint initiative

By

SCs & STs Research & Training Institute, Bhubaneswar

and

ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha.

Supported by

Ministry of Tribal Affairs (MoTA),

Government of India

2021

FOREWORD

Sickle cell disease is one of the most monogenic disorders globally. Sickle cell anaemia is a neglected chronic disorder of increasing global health importance. India is estimated to have the second highest burden of the disease. The sickle gene is widespread in tribal populations in India, which comprise the most socio-economically disadvantaged communities. Most of these tribal populations rely on local healing practices and refer to primary healthcare facilities at an advanced state of the disease. The Indian Council of Medical Research (ICMR) under its Tribal Health Research Forum (THRF) activities as well as other programs under the National Rural Health Mission (NRHM) in different states have initiated programs to address the issue appropriately.

The inbound and the outbound migrating tribal populations are potential carriers of the sickle gene and hence are the potential transmitters. Due to lack of ample awareness and information on the dreadfulness of sickle cell disease, these potential carriers pose threat to the wider community. Inadequate screening of the new-borns and children add to the existing concerns over spreading of sickle cell anaemia.

The public health implications of sickle-cell anaemia are significant. The most important challenge is, thus, to improve the prospects for the patients with sickle-cell anaemia in tribal areas. Sickle-cell anaemia can be prevented with appropriate measures and health education. In view of the scale of the public health problem, a comprehensive approach to prevention and management of sickle-cell anaemia is urgently needed.

In this context, this **Compendium of Evidence** provides a valuable window on research in the field of Sickle Cell Anaemia in India and covers the necessary components like prevalence, screening and diagnosis, treatment, reviews, case reports, programs and relevant other aspects. Focus has been laid upon reviewing the available literature so far on sickle cell disease related research involving the tribal population in India. Different search strategies were employed to explore, retrieve, collate, chronicle, comprehend relevant research and publications do as to gather a holistic body of information related to the sickle cell anaemia and its cross cutting thematic aspects. The compendium thus provides an information base related to sickle cell anaemia that would cater to the needs of researchers, physicians, academicians, policy makers and several others like NGOs and philanthropic organizations who have been working in the field to abate sickle cell anaemia in tribal areas of Odisha as well as in India.

The challenges in abating sickle cell anaemia are both difficult and stimulating. People have been working on them with enthusiasm, tenacity, and dedication to develop new methods of analysis and provide new solutions to keep up with the ever-changing threats. In an era when the government is proactively addressing tribal issues with adequate importance on securing health for development, the review of research on sickle cell anaemia will provide insights for purposeful and meaningful health related extension program; and will be a ready reckoner and handy reference towards designing customized programs for better quality care as well as social and genetic counselling support; for those tribal people with genetic disadvantages and their families. This Compendium is a good step in that direction.

This project has been supported by Ministry of Tribal Affairs (MoTA) to Scheduled Castes & Scheduled Tribes Research and Training Institute. The entire exercise has been jointly done by RMRC and SCSTRTI.

Smt. Ranjana Chopra, IAS
Principal Secretary, ST & SC Development, Minority &
Backward Classes Welfare Department, Govt. of Odisha

PREFACE

Sickle cell anaemia is the most common monogenetic disorder currently prevailing worldwide. Prevalence of the disease is high among the people of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean. Sickle Cell Disease (SCD) is one of the neglected health problems in India. Since the early 20th century, scientific and clinical research on sickle cell disease has resulted in the creation of a vast repository of scientific evidence on the disease. In the Indian context, significant research leads have been there on the disease guiding the programmatic directions towards abating sickle cell anaemia in the states and the country.

This Compendium of Evidence sets out to review the state of the art of research in the field of sickle cell anaemia in India, and to consider how existing research-based information contained in the publications can influence policy formulation and managerial decision-making towards abating sickle cell anaemia in tribal areas, especially in Odisha. The states like Madhya Pradesh, Maharashtra, Tamil Nadu, Andhra Pradesh, Uttar Pradesh, Gujarat, Kerala, Karnataka, Odisha and West Bengal have a reasonable load of sickle cell anaemia as studied from the prevalence of the disease. The sickle gene is widespread in tribal populations in most of the tribal-dominated states of the country towards which sickle cell anaemia control programs and initiatives have been operating in different states. In this context, this 'compendium of evidence' is an initiative towards contributing to the information need of policymakers and implementers by compiling, summarizing and analysing empirical studies on sickle cell disease in India.

The first part provides a broad introduction to the subject and the purpose. Aptly, the section describes the general aspects of sickle cell disease, types and prevalence, the gravity of sickle cell anaemia, objective and methodology. An extensive search mechanism was employed to gather relevant literature on the subject in the context of India. The searches were built on MESH terms and keywords with Boolean queries, and also considers the different approaches for capturing data.

Section 1 chronicles the titles and abstracts of research papers, articles, reviews and cases related to the prevalence of sickle cell diseases in the Indian population with the focus on prevalence in tribal areas. As many as 333 articles and studies have been reviewed and their abstracts have been presented. All the surveys, prevalence studies and cross-cutting studies under this theme have been covered. It provides for thinking about efficiency that seeks to reconcile the different perspectives.

In Section 2 the research on screening and diagnosis of sickle cell disease in the population of different age groups have been comprehended with abstracts of 118 research papers, studies and reviews. It is seen that most of the studies addressed prenatal and newborn screenings. The review of literature brings to fore many aspects of screening and diagnosis within a patient classification system.

Section 3 further explores the issue of comparing similar types of care but does so by exploring the use of treatment data for measuring efficiency as is evidenced in different kinds of literature. A total of 71 articles with the objective of treating or reducing any side effects from sickle cell disease have been reviewed and comprehended.

Section 4 covered the available theoretical, methodological, clinical and methodological reviews on the subject. A total of 73 reviews including narrative reviews, systematic reviews and overview of reviews were accessed, assessed and comprehended in the context of sickle cell anaemia in populations in India, especially the tribal population.

Section 5 describes case reports of treatments and procedures, clinical analysis of cases, regional variations, molecular characterization and diagnosis, etc. As many as 147 case reports were accessed and their abstracts prepared to provide a glimpse of typical research in the relevant subject and the resultant outputs. The case reports

were reported on individual patients. All the laboratory related studies, including biochemical tests, clinical profiles, hematology based tests have been categorized and classified in this chapter.

Section 6 provides a glimpse of comprehensive programs and in this section, as many as 18 programs related to sickle cell disease have been reviewed and comprehended. The different programs focused on different need-based aspects and reflected lessons learnt from the implementation and operationalization of such programs.

Section 7 covers many other studies, reports, papers and articles relevant to sickle cell disease which could not be classified as has been done for earlier chapters. As many as 111 literature have been placed in this chapter including case control studies, cohort studies, abstracts, epidemiology related studies, reflections from leaders, new perspectives, pilot studies, book chapters, retrospective studies, preliminary reports, trade documents, protocol papers, observational study, comorbidity study, qualitative study and registry.

The conclusion section summarizes all the evidence-based research purposefully classified for this compendium of evidence. It also discusses the different threads of the compendium and highlights its potential to create promising opportunities for developing effective programs towards addressing the issues of sickle cell disease and its abatement.

The motivation for this compendium is that – in different ways – policymakers, managers, politicians and the general public have profound concerns about the efficiency of the initiatives taken towards addressing the increasing load of sickle cell anaemia. The contents in the compendium may be useful for improving policy and managerial decisions to control and abate sickle cell anaemia. The compendium does not put forward a set of prescriptive policy or managerial interventions rather provides a vast body of research-based evidences for taking policy level decisions. We therefore hope that it provides a solid foundation for conceptualizing interventions in the sickle cell anaemia sector and related health systems and offers a good basis for those seeking to take concrete actions.

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ACKNOWLEDGEMENT

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In bringing out this Compendium of Evidence on research in the field of Sickle Cell Anaemia, I am indebted to the team of researchers, specialists, reviewers and design experts who worked relentlessly and collaboratively at Regional Medical Research Centre (RMRC), Bhubaneswar and at SCSTRTI, Bhubaneswar to make it possible.

We are especially indebted to Prof. (Dr.) A. B. Ota, IAS, Advisor-cum-Director & Special Secretary to Govt. SCSTRTI, Bhubaneswarfor his expert guidance and to his team members from SCSTRTI, Bhubaneswar. We are grateful to Dr. Bigyanananda Mohanty, Deputy Director and Ms. Moushumi Nayak, Assistant Director (R) who have been the coordinating links between RMRC and SCSTRTI for this project and contributing to the compilation on several counts. We are grateful to other staff of SCSTRTI, Bhubaneswar for their meaningful involvement without which this outcome would not have been as cherished.

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STUDY TEAM

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CONTENTS

EXECUTIVE SUMMARY

Sickle cell anaemia is the most common monogenic disorder currently prevailing worldwide. The disorder is highly prevalent among the people of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean. In India, sickle cell disease (SCD) is a neglected health problem, which explains why general research is scarce in this sector. Various haemoglobinopathies have been described since the early twentieth century. Australian and British pathologists initially investigated the prevalence of sickle-cell haemoglobin in India. Sickle cell haemoglobin is due to point mutation in the gene coding for one of the component proteins of haemoglobin causing an amino acid substitution. In the 1950s and 1960s, cross-sectional prevalence surveys across diverse tribes in India found prevalence, notably among tribal populations, with the wide variance within and among tribal communities, ranging from 1% to 40%–55%. Since then, the high prevalence of sickle cell haemoglobin has been reported among specific tribal populations, with a regionally higher incidence in numerous non-tribal and socially disadvantaged demographic groups, such as other backward classes and scheduled castes. Recent studies on Sickle Cell Disease/Trait are extensive, and these reviews have summarised the regional and population prevalence based on several cross-sectional surveys. The disease's prevalence in socially disadvantaged populations, which already face barriers to health care and inequities, necessitates a health-systems approach that goes beyond describing the prevalence and clinical features and tries to identify actionable gaps in the contextual understanding of the disease. Aside from infectious diseases and chronic diseases, genetic disorders such as Sickle cell disease are emerging as serious public health issues in India. In its most severe form, the illness is linked to chronic, life-altering, and life-threatening disorders, as well as health complications that can lead to disability or death.According to the NRHM's official website, Madhya Pradesh has the highest prevalence rate at 48.5%, followed by Maharastra at 45.4%, Tamil Nadu at 35.3%, Andhra Pradesh at 34.6%, Uttar Pradesh at 32.6%, Gujarat at 30%, Kerala at 29.7%, Karnataka at 25%, Odisha at 12.4%, and West Bengal at 1.1%. Due to a lack of knowledge, comprehensive programmes, and systematic methods to prevent the disorder, a substantial number of children in our country continue to be born and suffer from this condition. Due to the severity of the problem and the financial consequences of its management, appropriate control measures must be introduced urgently. The prevention strategies implemented for controlling the disease may be the primary or secondary methods. The primary preventive strategy is to identify the carriers and to avoid the marriage of carrier couples and the secondary prevention strategy is to use prenatal diagnostics to prevent the birth of the affected child. The challenge to control Sickle cell disorder is substantial and an integrated approach is required for both screening and management of the disorder.

The report is the outcome of the concerted efforts of the Regional Medical Research Centre, Bhubaneswar and Scheduled Castes and Scheduled Tribes Research and Training Institute, Bhubaneswar. The study is supported by the Department of SCST, Government of India in collaboration with the Ministry of Tribal Health, Government of India. The objective of the study is to collate the knowledge and research in the Sickle cell field and provide guidance to all concerned in this sector.

The present compendium of evidence highlights all the research which is carried out in the field of sickle cell involving the Indian population. The objective of this compendium is to collect all the research in the field of sickle cell in one place where evidence-based research will help the health care providers, government agencies and at the policy level to use this knowledge hub for the prevention and management of sickle cell disorders. It is an urgent need for a common platform where researchers from various domains such as Medicine, Public health, Biochemistry, Microbiology, Anthropology, and others may collaborate to find a cost-effective and substantial solution to sickle cell disorder. The compendium is divided into different themes Prevalence of disease, Screening and Diagnosis of disease, Treatment for disease, Reviews related to Sickle cell, Case reports, Programs related to sickle cell and rest other studies.

The compendium will serve as an evidence-based research collection that will update on all current research topics within this field. For this compendium, we have searched four databases which include Medline via PubMed, EMBASE via Ovid, Cochrane Library-CENTRAL and ProQuest. We have formulated different search strategies for different databases. We found a total of 13650 articles after the removal of duplicates which we included in

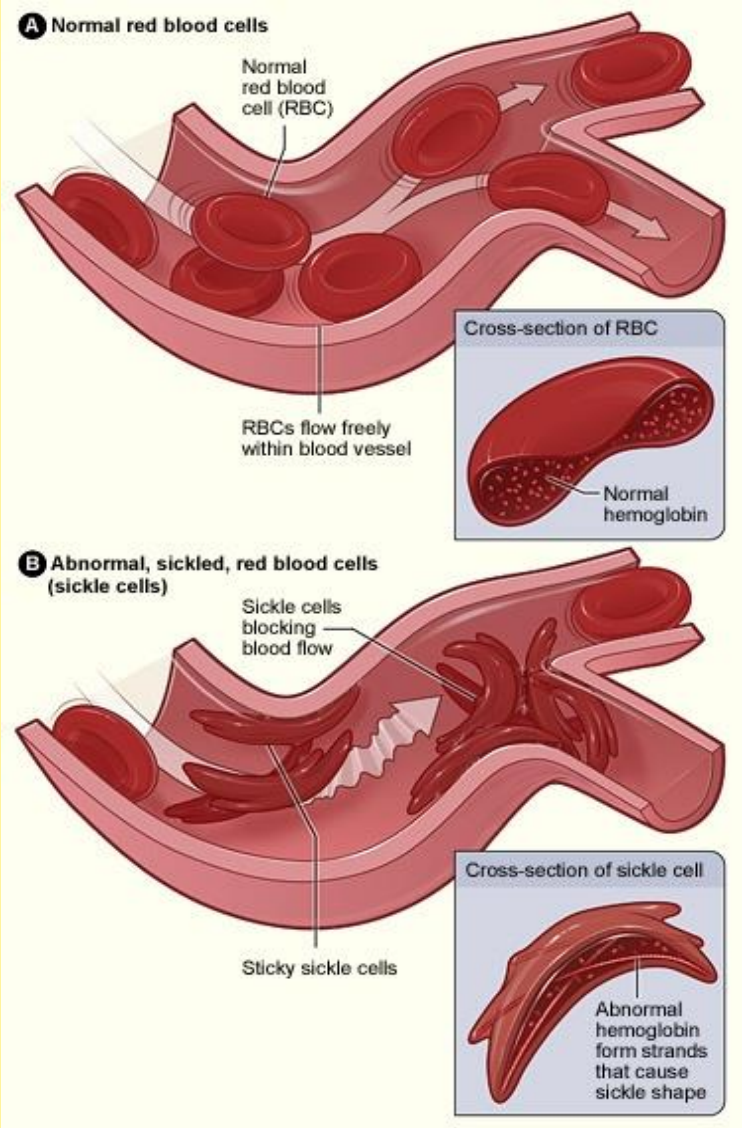
the initial title and abstract screen. After initial and comprehensive article screening, we found a total of 803 articles that were relevant to sickle cell among the population of Indian origin. After all, articles were screened we have divided the articles and studies into different themes. We have divided all the studies, articles and reviews into 6 different themes. We have categorized all the rest articles into the theme “Others”. The main themes identified were Prevalence, Screening and Disorder, Treatment, Reviews, Case reports, Programs and Others. We found a total of 286 articles/studies which were related to the prevalence or burden of sickle cell in India. We found 88 studies related to Screening and Diagnosis of sickle cell disease. We found 60 articles related to the treatment of sickle cell disease or disorders as the topic. We have included reviews like Narrative reviews, systematic reviews, Overviews of reviews where we found 50 studies. There were 196 case reports on Sickle cell topics from various parts of the country. We found 12 articles that were related to sickle cell programs in India. After classification of different articles and studies into different themes we have categorized all other articles into the theme “Others”, there were a total of 111 entries under this theme which included Authors' perspectives, epidemiological studies, newspaper articles, letters to the editor, book chapters, conference papers etc. were categorized. The following evidence compendium is being created to integrate the collected data into an action plan in which research from many domains and areas may be grouped under one broad objective with the primary aim of preventing and controlling sickle cell disease. This compendium will assist us in identifying knowledge gaps as well as link different works in the context of their contribution to the issue and other significant works in the same area. The report is a compilation of all the available research on the subject of Sickle cell disease in India structured in such a manner that it will help in answering any concern of health care professionals. This compendium of evidence will serve as the foundation of knowledge for sickle cell-related research in India.

ABBREVIATIONS

CBC- Complete Blood Count
GWAS- Genome-wide Association Studies
HBB- Hemoglobin Subunit Beta
HbS- Sickle Haemoglobin
Hb- Hemoglobinopathy
HPLC- High-Performance Liquid Chromatography
ICMR- Indian Council of Medical Research
IEF- Isoelectric Focusing
MeSH- Medical Subject Headings
MRI- Magnetic Resonance Imaging
MSH- Multicenter Study of Hydroxyurea
NPM- Neuro-psychometric
PROPS I & II- Prophylactic Penicillin Studies I and II
RMRC- Regional Medical Research Centre
RBC- Red Blood Cells
RCT- Randomized Clinical Trial
SCD- Sickle Cell Disease
SCA- Sickle Cell Anaemia
SCT- Sickle Cell Trait
SCSTRTI- Scheduled Castes and Scheduled Tribes Research and Training Institute
SNP- Single Nucleotide Polymorphism
STOP I - Stroke Prevention Trial in Sickle Cell Anemia
TCD- Transcranial Doppler ultrasonography

BACKGROUND

Sickle cell disease (SCD) is a group of blood disorders typically inherited from a person's parents. The most common type is known as sickle cell anaemia (SCA). It causesan abnormality in the oxygen-carrying capacity in the protein haemoglobin found in red blood cells. This leads to a rigid, sickle-like shape of the red blood cells under certain circumstances. Symptoms of sickle cell disease usually appear around the age of 5 to 6 months. Pain attacks, anaemia, swelling in the hands and feet, bacterial infections, and stroke are all possible health problems due to this disorder. People may acquire long-term as people get older.



Sickle cell disease is caused by a person inheriting two abnormal copies of the β-globin gene (*HBB*), one from each parent. This gene is found on chromosome 11. Depending on the particular mutation in each haemoglobin gene, there are several subtypes. Temperature fluctuations, stress, dehydration, and high altitude can all trigger an attack. A person with a single abnormal copy does not usually have symptoms and is said to have sickle cell trait. Such people are also referred to as carriers. A blood test is used to diagnose the disease, and some countries test all newborns for the disorder at birth. It's also possible to get a diagnosis while pregnant.

Infection prevention with vaccinations and antibiotics, increased water intake, folic acid supplementation, and pain medication are all available options for patients with sickle cell disease. Blood transfusions and the drug hydroxycarbamide are two more options (hydroxyurea). A transplant of bone marrow cells can be used in a small percentage of patients.

In summary, Sickle cell disorder is a term that refers to a group of inherited red blood cell disorders. Red blood cells are spherical and flow through small blood channels to transport oxygen to all regions of the body in a healthy state. Sickle cell disease causes red blood cells to become hard and sticky, resembling a C-shaped farm tool called a "sickle".

The early death of sickle cells results in a constant shortage of red blood cells. They also get stuck and obstruct blood flow when they travel through small blood arteries. This can result in pain as well as more serious issues like infection, acute chest syndrome, and stroke.

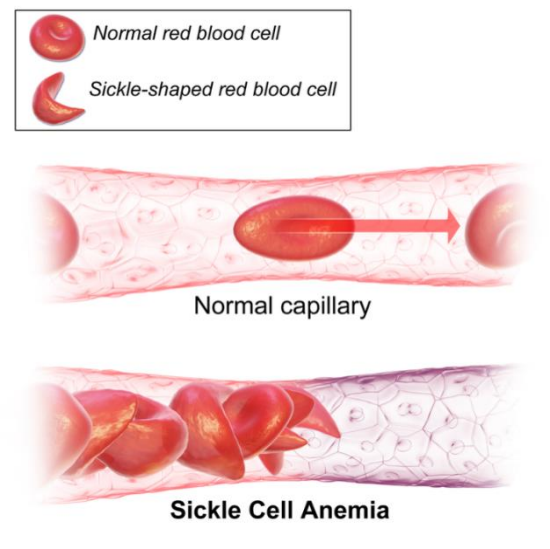
TYPES OF SCD

- **HbSS**

People who have this form of Sickle cell disorder inherit two sickle cell genes ("S"), one from each parent. This is also known as Sickle cell anaemia and is usually the most severe form of the disease.

- **HbSC**

People who have this form of Sickle cell disorder inherit a sickle cell gene ("S") from one parent and the other parent a gene for an abnormal haemoglobin called "C". This is usually a milder form of SCD.



- **HbS beta-thalassemia**

People who have this form of Sickle cell disorder inherit one sickle cell gene ("S") from one parent and one gene for beta-thalassemia, another type of anaemia, from the other parent. There are two types of beta-thalassemia: "0" and "+". Those with HbS beta 0-thalassemia usually have a severe form of Sickle cell disorder. People with HbS beta +-thalassemia tend to have a milder form of Sickle cell disorder.

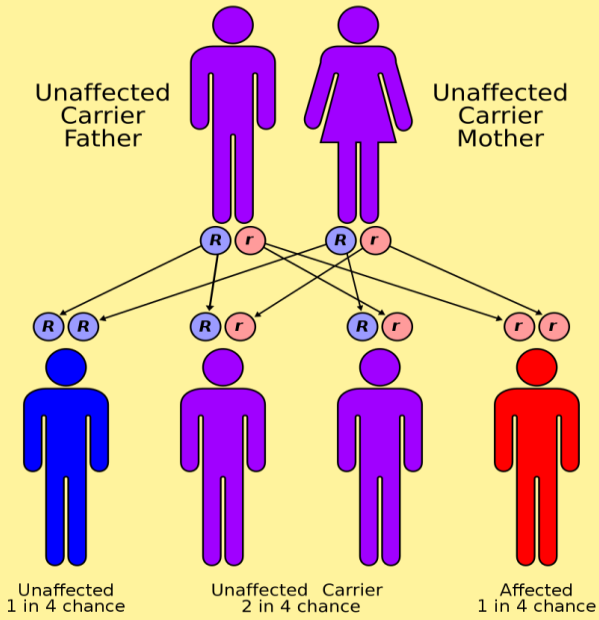
There also are a few rare types of Sickle cell disorders:

- **HbSD, HbSE, and HbSO**

People who have these forms of Sickle cell disorder inherit one sickle cell gene ("S") and one gene from an abnormal type of haemoglobin ("D", "E", or "O"). Haemoglobin is a protein that allows red blood cells to carry oxygen to all parts of the body. The severity of these rarer types of SCD varies.

- **Sickle Cell Trait (SCT)HbAS**

People who have the Sickle cell trait inherits one sickle cell gene ("S") from one parent and one normal gene ("A") from the other parent. This form is known as the Sickle cell trait (SCT). SCT patients normally show no symptoms of the condition and lead normal lives, although they can transmit the characteristic along to their children. In addition, there are a few unusual health issues that could be linked to sickle cell traits.



OBJECTIVE

To compile, summarize and carry out an analysis of empirical studies on sickle cell disease in India and create a compendium by evidence synthesis.

WHY INDIA?

SCD is found in high frequency in tropical regions, particularly Sub-Saharan Africa, India and the Middle East. Sickle cell anaemia is very widespread in India, especially in the tribal belts of Central and Southern India. Sickle cell anaemia is very widespread in India, especially in the tribal belts of Central and Southern India. Sickle cell anaemia is very widespread in India, especially in the tribal belts of Central and Southern India. Sickle cell anaemia has serious public health consequences, including worse quality of life, shorter life expectancy, and greater infant mortality rates. SCD is a major problem in India, with an estimated 5200 live births per year. Scheduled tribes, which have a high prevalence of socioeconomic deprivation and are usually medically underserved, have a Sickle Cell gene prevalence of 5 to 34 %. India also has a large population of tribal populations, estimated to be around 18 crores, with 1.80 crore sickle cell characteristics and 14 lakes with sickle cell disease. This demonstrates India's significant public health burden.

India has the largest concentration of tribal populations globally. They are believed to be the early settlers in the country and are considered to be the original inhabitants. According to the Census of India 2011, the tribal population of India is 8.6 per cent of the total population which is about 67.8 million people. The States of Madhya Pradesh, Maharashtra, Odisha, Gujarat, Rajasthan, Jharkhand, Chhattisgarh, Andhra Pradesh, West Bengal and Karnataka account for around 83 per cent of the total scheduled tribe population in the country and the majority of these tribal groups live in rural areas. In all, 705ethnic groups are listed as scheduled tribes and they have their characteristic cultural patterns, languages and social systems, by and large keeping to themselves. The following table shows the estimated prevalence in different states of India.

Sl. No.	State	Prevalence
1	Madhya Pradesh	0-48.5
2	Maharashtra	0-45.4
3	Tamil Nadu	0-35.3
4	Andhra Pradesh	0-34.6
5	Uttar Pradesh	0-32.6
6	Gujarat	0-30
7	Kerala	0-29.7
8	Karnataka	0-25
9	Orissa	0-12.4
10	West Bengal	0-1.1

*Sickle Cell Anemia Control Program | Initiatives | NHM (gujarat.gov.in)

METHODOLOGY

In this review, the particular focus of our searching mechanism was on Sickle-cell-related research involving the Indian population or in India.

We screened literature for relevance to SCD based in India as well as literature that assesses any SCD based literature having an Indian population. We identified peer-reviewed papers through searches in the following medical literature databases:

The searches were built on MESH terms and keywords with Boolean queries. The search builds is provided below each specific to each database and search engine. The studies were limited to the English language with no limits on the date of publication. We have included all peer-reviewed literature, Conference papers, posters, book chapters, and any news articles.

1. Medline via PubMed

2. EMBASE via Ovid

3. Cochrane Library-CENTRAL

4. ProQuest

The articles were retrieved into a reference management software and checked for duplication. Following this, 2 authors each used pre-defined criteria to screen all the articles for inclusion into the compendium and categorize them simultaneously into the following broad thematic groups-

1. Prevalence of Sickle Cell Disease

2. Screening and Diagnosis

3. Treatment

4. Case-reports

5. Programs

6. Reviews

7. Others

Disagreements were resolved by discussion and consensus. The screening and categorization were performed by using Rayyan software designed for this purpose. A supervisor reviewed 10% of the articles to ensure consistency and maintain quality.

The detailed search strategy used for different databases are as provided-

SEARCH STRATEGY: PUBMED

(((((("Anemia, Sickle Cell"[Mesh] OR "Anemias, Sickle Cell" OR "Sickle Cell Anemias" OR "Hemoglobin S Disease" OR "Disease, Hemoglobin S" OR "Hemoglobin S Diseases" OR "Sickle Cell Anemia" OR "Sickle Cell Disorders" OR "Sickle Cell Disorder" OR "HbS Disease" OR "Sickle Cell Disease" OR "Cell Disease, Sickle" OR "Cell Diseases, Sickle" OR "Sickle Cell Diseases")) OR ("Sickle cell")) OR ("sickle cell trait")) OR (Sickle Cell Trait[Mesh]) OR ("sickle cell trait*")) AND (("India"[Mesh] OR India[TIAB] OR "Uttar Pradesh"[TIAB] OR Maharashtra[TIAB] OR Karnataka[TIAB] OR Kerala[TIAB] OR Gujarat[TIAB] OR "Tamil Nadu"[TIAB] OR "West Bengal"[TIAB] OR "Andhra Pradesh"[TIAB] OR Rajasthan[TIAB] OR

Chhattisgarh[TIAB] OR "Madhya Pradesh"[TIAB] OR Bihar[TIAB] OR Punjab[TIAB] OR Assam[TIAB] OR Odisha[TIAB] OR Haryana[TIAB] OR "Jammu and Kashmir"[TIAB] OR Telangana[TIAB] OR Jharkhand[TIAB] OR Goa[TIAB] OR "Himachal Pradesh"[TIAB] OR "Arunachal Pradesh"[TIAB] OR Tripura[TIAB] OR Nagaland[TIAB] OR Sikkim[TIAB] OR Mizoram[TIAB] OR Manipur[TIAB] OR Meghalaya[TIAB] OR Uttarakhand[TIAB] OR "Andaman & Nicobar Islands"[TIAB] OR Chandigarh[TIAB] OR "Dadra & Nagar Haveli"[TIAB] OR "Daman & Diu"[TIAB] OR Delhi[TIAB] OR Lakshadweep[TIAB] OR Puducherry[TIAB] OR Ladakh[TIAB]))

SEARCH STRATEGY: PROQUEST

(mesh.Exact("Anemia, Sickle Cell" OR "Sickle Cell Trait" OR "Hemoglobin, Sickle") OR mainsubject.Exact("anemia, sickle cell - psychology" OR "sickle cell trait" OR "anemia, sickle cell" OR "sickle cell anaemia" OR "sickle cell anemia" OR "sickle cell disease") OR ("sickle cell* " OR "sickle cell trait*" OR "sickle cell disease*" OR "sickle cell disorder*" OR "sickle cell anaemia*" OR "sickle cell anemia*" OR hemoglobinopath* OR haemoglobinopath*)) AND(mesh.Exact("India") OR mainsubject.Exact("india") OR ("India*" OR ("Uttar Pradesh" OR Maharashtra OR Karnataka OR Kerala OR Gujarat OR Tamil Nadu OR "West Bengal" OR "Andhra Pradesh" OR Rajasthan OR Chhattisgarh OR "Madhya Pradesh" OR Bihar OR Punjab OR Assam OR Odisha OR Haryana OR "Jammu and Kashmir" OR Telangana OR Jharkhand OR Goa OR "Himachal Pradesh" OR "Arunachal Pradesh" OR Tripura OR Nagaland OR Sikkim OR Mizoram OR Manipur OR Meghalaya OR Uttarakhand OR “Andaman & Nicobar Island*” OR Chandigarh OR “Dadra & Nagar Haveli” OR “Daman & Diu” OR Delhi OR Lakshadweep OR Puducherry OR Ladakh)))

SEARCH STRATEGY: COCHRANE

((MeSH descriptor: [Anemia, Sickle Cell] explode all trees OR MeSH descriptor: [Sickle Cell Trait] explode all trees OR MeSH descriptor: [Hemoglobin SC Disease] explode all trees OR MeSH descriptor: [Hemoglobin, Sickle] explode all trees OR "sickle cell" OR "Sickle Cell Anemia*" OR "sickle Cell anaemia" OR "Hemoglobin S Disease*" OR "Sickle Cell Disease*" OR "Cell Diseases, Sickle" OR "Disease, Hemoglobin S" OR "HbS Disease*" OR "Cell Disease, Sickle" OR "Sickle Cell Disorders" OR "Sickle Cell Disorder" OR "Sickle Cell Disease" OR "Sickle Cell Diseases" OR Cell Disorders, Sickle OR Anemias, Sickle Cell OR Cell Disorder, Sickle OR Disease, Hemoglobin S) AND (MeSH descriptor: [India] explode all trees OR India OR "Uttar Pradesh" OR "Maharashtra" OR "Karnataka" OR "Kerala" OR "Gujarat" OR "Tamil Nadu" OR "West Bengal" OR "Andhra Pradesh" OR "Rajasthan" OR "Chhattisgarh" OR "Madhya Pradesh" OR "Bihar" OR "Punjab" OR "Assam" OR "Odisha" OR "Haryana" OR "Jammu and Kashmir" OR "Telangana" OR "Jharkhand" OR "Goa" OR "Himachal Pradesh" OR "Arunachal Pradesh" OR "Tripura" OR "Nagaland" OR "Sikkim" OR "Mizoram" OR "Manipur" OR "Meghalaya" OR "Uttarakhand" OR “Andaman & Nicobar Islands” OR "Chandigarh" OR “Dadra & Nagar Haveli” OR “Daman & Diu” OR "Delhi" OR "Lakshadweep" OR "Puducherry" OR "Ladakh" OR "South india*"))

SEARCH STRATEGY: PSYCINFO

((exp Sickle Cell Disease/ OR Sickle Cell Disease$.tw. OR Anemias, Sickle Cell.tw. OR Sickle Cell Anemia$.tw. OR Hemoglobin S Disease$.tw. OR Disease, Hemoglobin S.tw. OR Sickle Cell Disorder$.tw. OR HbS Disease$.tw. OR Cell Disease, Sickle.tw. OR Cell Diseases, Sickle.tw.) AND (India$.tw. OR Uttar Pradesh.tw. OR Maharashtra.tw. OR Karnataka.tw. OR Kerala.tw. OR Gujarat.tw. OR Tamil Nadu.tw. OR West Bengal.tw. OR Andhra Pradesh.tw. OR Rajasthan.tw. OR Chhattisgarh.tw. OR Madhya Pradesh.tw. OR Bihar.tw. OR Punjab.tw. OR Assam.tw. OR Odisha.tw. OR Haryana.tw. OR Jammu & Kashmir.tw. OR Telangana.tw. ORJharkhand.tw. OR Goa.tw. OR Himachal Pradesh.tw. OR Arunachal Pradesh.tw. OR Tripura.tw. OR Nagaland.tw. OR Sikkim.tw. OR Mizoram.tw. OR Manipur.tw. OR Meghalaya.tw. OR Uttarakhand.tw. OR Andaman & Nicobar Islands.tw. OR Chandigarh.tw. OR Dadra & Nagar Haveli.tw. OR Daman & Diu.tw. OR Delhi.tw. OR Lakshadweep.tw. OR Puducherry.tw. OR Ladakh.tw. OR South india$.tw.))

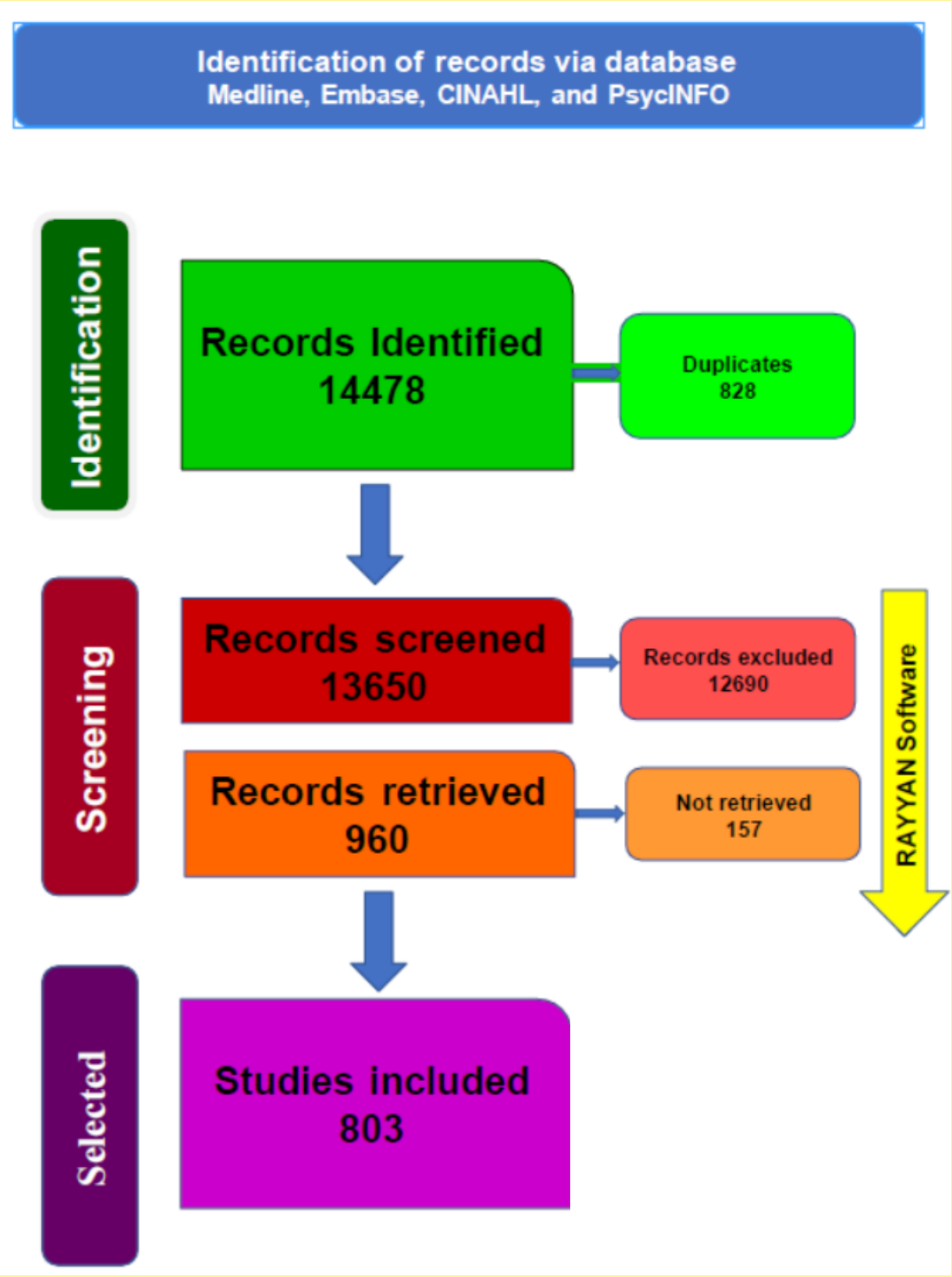
SEARCH STRATEGY: CINAHL

(((MH "Anemia, Sickle Cell+") OR Tl Hemoglobin S Disease* OR AB Hemoglobin S Disease* OR Tl Sickle Cell Anemia* OR AB Sickle Cell Anemia* OR Tl Anemia, Sickle Cell OR AB Anemia, Sickle Cell OR Tl Sickle Cell Disease* OR AB Sickle Cell Disease* OR Tl Cell Diseases, Sickle OR AB Cell Diseases, Sickle OR Tl Disease, Hemoglobin S OR AB Disease, Hemoglobin S OR Tl Cell Disease, Sickle OR AB Cell Disease, Sickle OR Tl HbS Disease* OR AB HbS Disease* OR Tl Sickle Cell Disorder* OR AB Sickle Cell Disorder*) AND ((MH "India") OR Tl India* OR AB India* OR Tl Andhra Pradesh OR AB Andhra Pradesh OR Tl West Bengal OR AB West Bengal OR Tl Tamil Nadu OR AB Tamil Nadu OR Tl Gujarat OR AB Gujarat OR Tl Kerala OR AB Kerala OR Tl Maharashtra OR AB Maharashtra OR Tl Maharashtra OR AB Maharashtra OR Tl Uttar Pradesh OR AB Uttar Pradesh OR Tl Jammu and Kashmir OR AB Jammu and Kashmir OR Tl Haryana OR AB Haryana OR Tl Odisha OR AB Odisha OR Tl Assam OR AB Assam OR Tl Punjab OR AB Punjab OR Tl Bihar OR AB Bihar OR Tl Madhya Pradesh OR AB Madhya Pradesh OR Tl Chhattisgarh OR AB Chhattisgarh OR Tl Rajasthan OR AB Rajasthan OR Tl Mizoram OR AB Mizoram OR Tl Sikkim OR AB Sikkim OR Tl Nagaland OR AB Nagaland OR Tl Tripura OR AB Tripura OR Tl Arunachal Pradesh OR AB Arunachal Pradesh OR Tl Himachal Pradesh OR AB Himachal Pradesh OR Tl Goa OR AB Goa OR Tl Jharkhand OR AB Jharkhand OR Tl Telangana OR AB Telangana OR Tl Lakshadweep OR AB Lakshadweep OR Tl Delhi OR AB Delhi OR Tl Daman & Diu OR AB Daman & Diu OR Tl Dadra & Nagar Haveli OR AB Dadra & Nagar Haveli OR Tl Chandigarh OR AB Chandigarh OR Tl Andaman & Nicobar Islands OR AB Andaman & Nicobar Islands OR Tl Uttarakhand OR AB Uttarakhand Tl Meghalaya OR AB Meghalaya OR Tl Manipur OR AB Manipur OR Tl South india* OR AB South india* OR Tl Ladakh OR AB Ladakh OR Tl Puducherry OR AB Puducherry))

SEARCH STRATEGY: EMBASE

(('sickle cell anemia'/exp OR 'sickle cell anemia' OR 'hemoglobin s disease' OR 'hemoglobin sc disease'/exp OR 'hemoglobin sc disease' OR 'sickle cell disorder*' OR 'hbs disease' OR 'cell disease, sickle') AND ('india'/exp OR india OR 'uttar pradesh'/exp OR 'uttar pradesh' OR 'karnataka'/exp OR karnataka OR 'maharashtra'/exp OR maharashtra OR 'kerala'/exp OR kerala OR 'gujarat'/exp OR gujarat OR 'tamil nadu'/exp OR 'tamil nadu' OR 'west bengal'/exp OR 'west bengal' OR 'andhra pradesh'/exp OR 'andhra pradesh' OR 'rajasthan'/exp OR rajasthan OR 'chhattisgarh'/exp OR chhattisgarh OR 'madhya pradesh'/exp OR 'madhya pradesh' OR 'bihar'/exp OR bihar OR 'punjab india'/exp OR 'punjab india' OR 'assam'/exp OR assam OR 'odisha'/exp OR odisha OR 'haryana'/exp OR haryana OR 'jammu and kashmir'/exp OR 'jammu and kashmir' OR 'telangana'/expOR telangana OR 'jharkhand'/exp OR jharkhand OR 'goa'/exp OR goa OR 'himachal pradesh'/exp OR 'himachal pradesh' OR 'arunachal pradesh' OR 'tripura'/exp OR tripura OR 'nagaland'/exp OR nagaland OR 'sikkim'/exp OR sikkim OR 'mizoram'/exp OR mizoram OR 'manipur'/exp OR manipur OR 'meghalaya'/exp OR meghalaya OR 'uttarakhand'/exp OR uttarakhand OR 'andaman & nicobar islands' OR 'andaman & nicobar islands' OR 'chandigarh'/exp OR chandigarh OR 'dadra & nagar haveli' OR 'national capital territory of delhi'/exp OR 'national capital territory of delhi' OR delhi OR 'lakshadweep'/exp OR lakshadweep OR 'puducherry'/exp OR puducherry OR ladakh))

The search results flow chart is provided below.



SUMMARY OF FINDINGS

Sickle cell disease (SCD) is one of the most common monogenic disorders found globally with an autosomal recessive inheritance. In 1910, a physician named James Herrick described the sickle-shaped red cells in a medical student from Grenada. Linus Pauling and his colleagues were the first to identify sickle haemoglobin (HbS) as a molecular illness in 1949, after demonstrating that it had abnormal electrophoretic mobility. Vernon Ingram discovered that sickle haemoglobin was caused by a single amino acid alteration in the haemoglobin molecule in 1957. A single base mutation in the triplet encoding the sixth residue of the -globin chain causes valine substituting for glutamic acid, resulting in the aberrant haemoglobin S (HbS), disease.

The basic pathophysiology is based on deoxyHbS polymerization and the production of long fibres within RBCs, resulting in a distorted sickle shape, which leads to increased haemolysis and sickle red cell vaso-occlusion. However, the clinical presentation in SCD patients varies greatly and triggers an event that might result in vaso-occlusion. Recent research has revealed the relevance of red cell dehydration, aberrant RBC adherence to the vascular endothelium, inflammatory processes, arterial activation, and nitric oxide metabolism anomalies in the pathophysiology of this multi-organ disease. Balanced polymorphism can be seen in the sickle gene. Heterozygotes have a selection advantage and are protected from Plasmodium falciparum malaria, but homozygotes have a higher rate of premature death.

Madhya Pradesh, Maharashtra, Odisha, Gujarat, Rajasthan, Jharkhand, Chhattisgarh, Andhra Pradesh, West Bengal, and Karnataka account for around 83 percent of the country's total scheduled tribe population, with the majority of these tribal communities living in rural areas. "Several thousand years ago, the entire subcontinent underwent a period of massive intermarriage, shuffling its population's genetic deck so thoroughly that it left clear traces even in the genomes of today's most isolated tribes," Reich and colleagues concluded.

The major tribal communities in central India are the Gonds and Bhils. The sickle gene is found in all of Maharastra’s eastern districts. The prevalence of sickle cell disease varies between tribes, with a high prevalence of the sickle disease among Bhils, Madias, Pawaras and Otkars.The whole tribal population of 1,25,000 people in Kerala's Wayanad district was screened, followed by genetic counselling in which HbS carriers were urged not to marry other HbS carriers.High prevalence was found among these populations (18.2-34.1 %). The Dhodia, Dubla, Gamit, and Naika tribes in Gujarat have a high frequency of HbS. (13-31 %). The Indian Red Cross Society, Gujarat State Branch, recently conducted large demographic surveys in which 1,68,498 tribals from 22 districts were checked and the overall prevalence of sickle cell carriers was 11.37 %. Chaudry, Gamit, Rohit, Vasava, and Kukuna tribal communities in south Gujarat have a high prevalence of HbS (6.3 to 22.7%) as well as the -thalassaemia trait (6.3 to 13.6%). Both of these genes are likely to be passed down in these ethnic groupings.
The HbS allele frequency ranged from 0.011 to 0.120 in a large multicentre study that tested 15200 individuals from 14 primitive tribes in Maharashtra, Gujarat, Tamil Nadu, and Odisha. The β- thalassaemia allele frequency ranged from 0.005 to 0.024. In this study, associated iron deficiency was found in 26.2 % of sickle heterozygotes and 67.7% of sicklehomozygotes. Kaur et al. analysed the prevalence of HbS in various tribal groups throughout various states. Although a large number of tribal groups have been screened for HbS, there are still major gaps in our understanding of the HbS gene's distribution in Indian tribal societies.

Among the Nilgiri hills of South India, Lehman and Cutbush described sickle haemoglobin in the indigenous community in 1952. Dunlop and Mazumder found sickle haemoglobin among Assam tea garden workers, who were mostly migrants from tribal communities in Bihar and Odisha. Since then, many populations, particularly tribal populations, have been examined, and sickle cell genes have been discovered in three socioeconomically backward ethnic groups in India: scheduled tribes, scheduled castes, and other backward classes.

Screening is used to detect potential health problems who have not yet exhibited any symptoms. Screening tests are distinct from diagnostic tests which are designed to identify the subset of the population that will require additional testing to ascertain whether or not they have a disease.

People who are unsure if they have a sickle or defective haemoglobin can get their blood tested to find out. They will be able to determine whether they have a gene or a characteristic that causes abnormal haemoglobin. Parents will be better educated about the likelihood of having a child with sickle cell disease through these tests.

NEWBORN SCREENING

When a child has sickle cell disease, it's critical to get a diagnosis as soon as possible so that complications can be avoided. Newborn screening programmes also check for an abnormal haemoglobin trait in the infant. If this is the case, the parents are notified, and counselling is offered.

PRENATAL SCREENING

Sickle cell disease can be diagnosed before a baby is born. A sample of amniotic fluid, the liquid in the sac around a growing embryo, or tissue from the placenta, the organ that connects the umbilical cord to the mother's womb, is used to do this. Prenatal testing is possible as early as 8 to 10 weeks into the pregnancy. Rather than abnormal haemoglobin, this test looks for the sickle haemoglobin gene.

While screening tests are not always accurate, it is generally more helpful to have them at the right times. Several study designs could be employed to assess the efficacy of screening. Correlational studies, for example, investigate changes in disease-specific mortality over time and correlate them with the frequency of screening in a community. Case-control and cohort studies are widely used to evaluate screening, although the research groups may not be similar due to confounders, volunteer bias, lead-time bias, and length-of-time bias. Because of these constraints, the best way to assess the performance of a screening programme is to undertake a randomised clinical trial (RCT) with a big enough sample size to assure control of potential confounding factors.

A diagnostic test is a process used to confirm or establish the existence of the disease in a person suspected of having a disease, usually after symptoms have been reported or based on the findings of previous medical tests. A non-experimental cross-sectional study that compares a test's categorization of a diagnosis with the classification of a reference standard in a relevant study population is the most appropriate study design for examining the accuracy of diagnostic tests. Basic diagnostics such as total blood count, reticulocyte count, and regular biochemistry tests such as LFT and RFT help monitor patients. Other tests, such as Transcranial Doppler ultrasonography (TCD), Magnetic Resonance Imaging (MRI) with or without angiography, and Neuropsychometric (NPM) examinations, may be performed.

The core concepts of preventative care for children with sickle cell disease include the prevention of infections by encapsulated organisms caused by functional asplenia. Pneumococcal immunisation and penicillin prophylaxis are beneficial to these patients. Other issues can be avoided by using Hydroxyurea and using blood transfusions.

THEMATIC RESULTS

We found a total of 803 articles and case reports which included Sickle cell-related topics in the Indian context. We have divided all the screened articles into 7 subthemes

1. Prevalence- 286
2. Screening and Diagnosis- 88
3. Treatment- 60
4. Reviews- 50
5. Case report- 196
6. Programs- 12
7. Others- 111

Section-1 Prevalence

In the Prevalence theme, we found 286 articles and studies. We have included all the surveys, prevalence studies and cross-sectional studies under this theme. All the relevant records are added in the Compendium of evidence section. The records were further categorized in the Indian and Odisha context. The cross-sectional surveys/studies included in the theme mainly looks at the data from the population at a specific point of the time. The studies were observational in nature and the research carried out in these describe the characteristics existing in the community. These studies are often used to make inferences about possible relationships or to gather preliminary data to support further research and experimentation. We found a total of 286 records out of which 30 records were from Odisha.

Section-2 Screening and Diagnosis

In the screening and diagnosis theme, we found 88 articles. The articles were mainly addressed to prenatal and newborn screenings. In this section, records were included which were related to screening and diagnosis of Sickle cell condition in India. The screening studies included all the records which included methods, technique, procedure, and examination for early and rapid detection of sickle cell disease in the population. The diagnosis studies were records that included the process of identifying the disease, condition or injury from its sign and symptoms. This also included the process including health history, case history, physical examination and diagnostic tests such as blood tests, imaging tests and biopsies which all help in diagnosis. Out of total of 88 records we found 8 records related to Odisha. The detailed records are given in the section Compendium of evidence section.

Section-3 Treatment

We found 60 articles with the objective of treating or reducing any side effects from sickle cell disease. The records included in this theme were research studies performed in people that are aimed at evaluating a medical, surgical or behavioural intervention. The treatments used can help manage the disease. The use of medicine, therapy, surgery and other treatments helps in reducing the symptoms and effects of the disease. We found 5 studies from Odisha in this context.

Section-4 Reviews

The review articles are also known as literature reviews, it is a survey of previously published research on a topic. The overview of all the research to the particular research gives the critical evaluation of all the data from existing studies. The review articles identify potential research areas to explore and to draw new conclusions from existing data. We found a total of 50 reviews which included narrative reviews, systematic reviews, and overview of reviews. The records are included in the section Compendium of evidence.

Section-5 Case reports

An article that describes and interprets an individual case, often written in the form of a detailed story. Case reports often describe; Unique cases that cannot be explained by known diseases or syndromes; Cases that show an important variation of a disease or condition; Cases that show unexpected events that may yield new or useful information; Cases in which one patient has two or more unexpected diseases or disorders. Case reports are considered the lowest level of evidence, but they are also the first line of evidence because they are where new issues and ideas emerge. There were 196 case reports. The case reports were reported from individual patients. The individual reports were categorized under the case report's theme. From Odisha, we found 24 case reports.

Section-6 Programs

The theme Program includes research related to health programs related to sickle cell disease and which include individual and organizational level strategies and interventions that influences health. The program works as an informational approach directed towards change. We found 12 studies that were related to programs or projects related to sickle cell disease.

Section-7 Others

We have categorized all other articles, studies, abstracts and letters into the Others category. In the Others category, we have 111 publications which included case-control studies, Cohort studies, Abstracts, Epidemiology related studies, Letter to the editor, Perspectives, Clinical trials, News topics, Anthropology studies, Short communications, Pilot studies, Book chapters, Retrospective studies, Poems, Preliminary reports, Trade documents, Comments, Protocol papers, Perspectives, Observational study, Comorbidity study, Registry and Qualitative study. The detailed records are classified into Indian and Odisha context in Compendium of evidence section.

The studies were again categorized into Odisha specific studies in which we found 73 studies. The distribution of studies is provided in the table below-

	Themes	Odisha	India
1	Prevalence	30	286
2	Screening and diagnosis	8	88
3	Treatment	5	60
4	Review	1	50
5	Case report	24	196
6	Programs	-	12
7	Others	5	111

The distribution percentage of all the identified records in India is provided in figure 1 and for Odisha is given in figure 2

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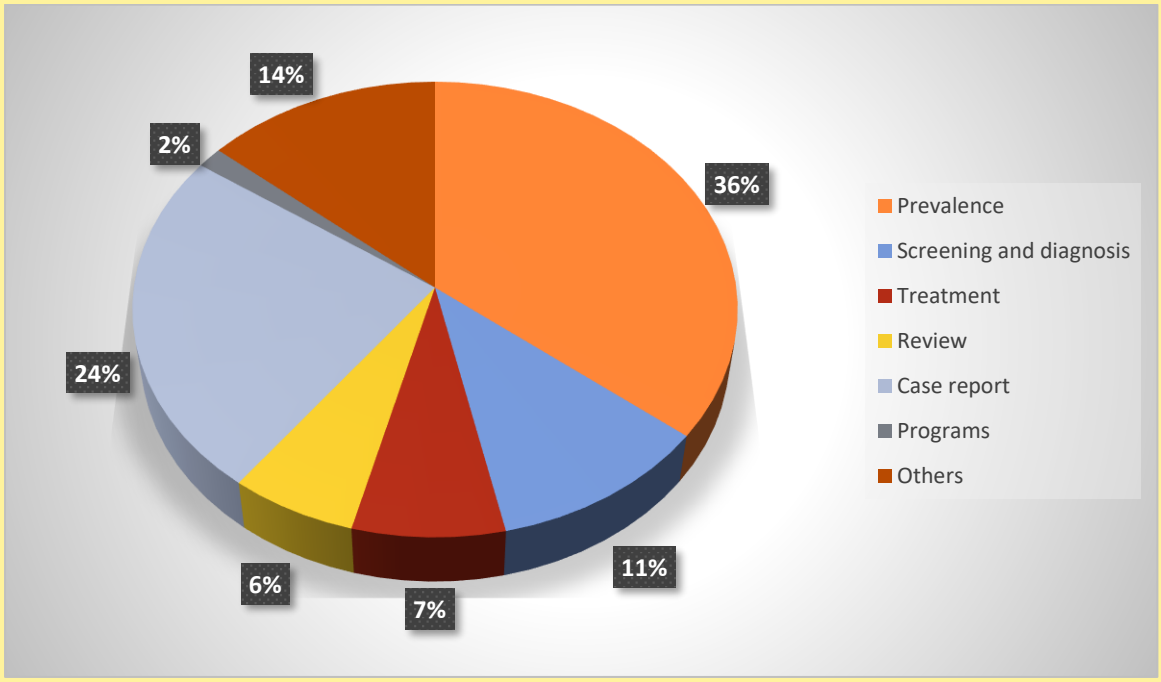

Figure 1- Thematic distribution of all publications relevant to the Indian population

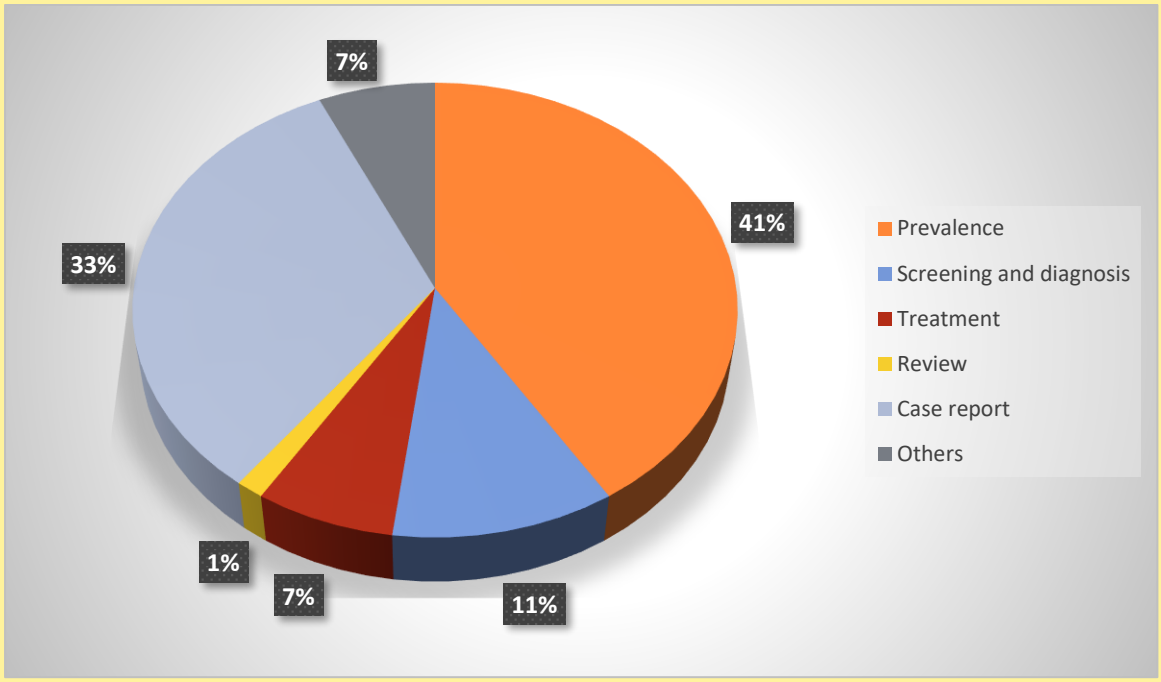

Figure 2- Thematic distribution of studies conducted in Odisha

Importance

Over the past five decades, there has been remarkable progress in the field of sickle cell disease research in India not only to analyze its determinants, rather find out the effective and cost-effective means for diagnosis and management of such life-threatening conditions. However, as more data and pieces of evidence are evolved dramatically, it is cumbersome to understand how, when and why to translate these researches into practice. The compendium summarizes key information regarding disease burden, its determinants and detrimental consequences, proven therapies and evidence-based health care such as newborn screening, health education, prophylaxis for education, optimal nutrition and hydration, blood transfusion, hydroxyurea therapy etc. for reduction of sickle cell-related adverse effects (e.g., pain crisis, acute chest syndrome, hospitalization, mortality and so on), which will help different national and subnational stakeholders to make the best use of the available evidence for designing and implementing an acceptable, affordable, appropriate and sustainable policy and program to prevent and control SCD. In addition, such compendium plays a vital role in drawing the portrait of sickle cell disease research to analyze the research trend, actors, focus and funding sources through bibliometric analysis. Furthermore, this compendium of evidence will be beneficial for researchers to identify several gaps that need further attention for improvising the understanding of biological as well as the social aspect of such incurable disease in a middle-income country like India.

Limitation

In this compendium, we could not determine the quality of the publications which is one of the major limitations of this compendium..The publications which were written in English were included in the study, as English is India's primary language for scientific communication and is solely utilised in health literature. SCD is a wide and interdisciplinary field, and while we used a broad search technique, potential peripheral topics of importance may have been missed. Similarly, a considerable amount of non-indexed journals and grey literature has not been examined.

CONCLUSION

This compendium of evidence has summarized all the published literature on SCD in India from 1952 to 2021 under different themes. The research output on SCD in India is low with only 803 total research-related publications. In this compendium, we have included all original articles, reviews, notes, conference papers, letters, book chapters etc relevant to the Indian context. We found over half of the investigations as observational studies and most of them were cross-sectional studies/surveys. There were very limited studies that evaluated any programs related to sickle cell disease in India. There were very few experimental studies related to sickle cell disease in India which is a cause of concern because these studies provided a high level of evidence in public health. The significant resources required to conduct longitudinal and experimental studies is probably a reason for this. This compendium can be used as a comprehensive strategy to formulate any sickle cell-related programs where every theme will be used as a strategy to combat this genetic condition. There is also a need to continuously update this compendium where all the new research will be added to the predefined themes and the knowledge hub will be used as a key tool in the prevention and management of sickle cell disease

To summarise, our analysis of SCD related publications from India between 1952 and 2021 reveals a significant rise in recent years. There are still significant opportunities to enhance the research outputs and SCD ecosystem in India. Existing gaps may be addressed by broadening the scope of research, forming partnerships, and including native groups and population-based studies.

COMPENDIUM OF EVIDENCE

INDIA

In this section, all the records are added except records from Odisha

PREVALENCE

1. **Cirrhosis in untreated sickle cell disease: Protein profile and outcomes**

   2015

   Indian Journal of Gastroenterology

   Sharma, H and Mishra, H and Gupta, N

Background: Sickle cell disease has a significant prevalence in central India (homozygous=0.6 %). There is little data about chronic liver disease apart from episodes of jaundice with cholestasis and hepatic sequestration. Study Design: Profiled consecutive patients of sickle cell disease with jaundice and ascites were studied. Results: Between June 2014 and June 2015, 87 patients (62 males/15 females) presented with jaundice and ascites. Mean age was 41.2Â±4 years (range 14-56 years). There was evidence of significant proteinuria (>300 mg/day). All had prior episodes of jaundice. Palpable left lobe of the liver with esophageal varices was seen in 58. Radiologically, features of cirrhosis were seen in 71. Splenic atrophy was seen in all. The reason for jaundice was HEV in 15 and hemolytic crisis in 48. Eight patients had prolonged cholestasis. There was evidence of spontaneous bacterial peritonitis in 7 patients. Three patients developed altered sensorium initially suspected as encephalopathy; however, there was rapid deterioration and one documented brain stem stroke. All patients were homozygous for sickle cell traits. Mortality at 1 month was significantly high in those with varices (31/58 vs. 3/29). No variceal bleed was encountered. Conclusion: Chronic liver disease in Indian patients with sickle cell disease (in the absence of hemosiderosis) has distinct characteristics with evidence of portal hypertension and concurrent renal involvement. In the presence of portal hypertension, there is significant short-term mortality.

2. **Î²-thalassaemia and its co-existence with haemoglobin E and haemoglobin S in upper Assam Region of north eastern India: A hospital based study**

   2016

   Journal of Clinical and Diagnostic Research

   Teli, A B and Deori, R and Saikia, S P and Pathak, K and Panyang, R and Rajkakati, R

Introduction: Î²-Thalassaemias are common genetic disorders in the Indian subcontinent and its status has not been well studied in the Upper Assam region of North Eastern India. Aim: The aim of the study was to show the prevalence of Î²- thalassaemias and its co-existence with Haemoglobin E and Haemoglobin S in the Upper Assam region of North Eastern India. Materials and Methods: A total of 1200 anaemic patients were investigated for Î²-thalassaemias. Complete Blood Count (CBC) and High Performance Liquid Chromatography (HPLC) were done for screening. Results: Out of 1200 patients screened, 5.83% Î²-thalassaemia trait, 2.33% compound Hb E/Î²-Thalassaemia, 1.33% Î²-thalassaemia major and 0.42% compound Hb S/Î²- thalassaemia were detected. A high incidence of thalassaemia is found among the people of Upper Assam region of North Eastern India. Conclusion: The only way to prevent the disease is carrier detection and awareness among the people about it.

3. **Prevalence and profile of device associated infection in precisely tribal sickle cell disease children above 10 years of age admitted to icu of a tertiary care hospital of tribal area**

   2021

   Indian Journal of Public Health Research and Development

   Subudhi, M and Jagatheeswary, P A T and Das, S K and Swain, A and Rout, R R

Background:Sickle cell disease (SCD) children are more susceptible to bacterial infection due to multifactorial cause with poorimmunization status in tribal area.Device associated infections (DAIs), due to extensive use of invasive devices in intensive care units, further increases morbidity and mortality in these patients. In the present study,our aim is to define, the total burden and profile of DAI as presentation, spectrum of bacterial isolate and susceptibility in SCD children, in specific to, ICU of a tertiary care Hospital in Tribal area. Methodology: This prospective study was conducted overDevice Associated infections (DAIs) in Sickle cell disease (SCD) tribal children, having an inserted indwelling device, in the ICU of atertiary care hospital.Demographic,clinical and date of device insertion data were recorded. Depending on the type of specimen, samples were cultured and analyzed.Antimicrobial susceptibility testing was performed on different isolates. Result: Out of 31 exposed SCD children to indwelling devices,the confirmed DAI cases were, 1 central line-associated bloodstream infections (CLABSI), 1 ventilator-associated pneumonia (VAP), and 3 catheter-associated urinary tract infections (CAUTI). The overall DAI rate was 16.1% with 29.7 per 1000 device days. The Organism causing infection were Gram-negative in 3(60%) cases, Gram-positive in 2 (40%), and as mixed infection with fungal organisms in 2(40%) cases. Most isolates were susceptible to Co-Trimoxazole, Ceftriaxone and Gentamycin. CONS and Klebsiella were showing multidrugresistant to more antibiotics tested.Conclusion:Since,In view of high DAIrate in Sickle cell Disease Tribal children in the ICU of tribal area,the preventive strategies should be plannednot only to improve immunity but also reduce morbidity,mortality, to ensure a good quality health care in them.

4. **Assessment of inflammatory markers in hemolytic crisis with special reference to sickle cell Anemia**

   2019

   Indian Journal of Public Health Research and Development

   Nigam, P and Patra, P K and Singh, L and Murthy, R

As a global health problem sickle cell anemia affects many world populations. It is an autosomal recessive disease, commonly found in tropical countries. It is the most common single genetic mutation in human and abundantly present in large part of the world. The present study was done in the Department of Biochemistry, Chhattisgarh Institute of Medical Sciences, Bilaspur. The work comprised of two different groups consisting 50 sickle cell patients with hyperhemolytic crisis, including 50 age and sex matched control subject. In the present study namely, Homosysteine, IL-6,TNF-a, and CRP as an inflammatory markers measured in normal and sickle cell disease patients. We found significantly increased mean level of all three parameters (IL â€“ 6 Group I V/s Group II p <0.001, TNF-Î± Group I V/s Group II p < 0.001,CRP Group I V/s Group II p <0.001). when compared to control and subject group.

5. **Prevalence of hemoglobinopathies in northeast India**

   2015

   Indian Journal of Physiology and Pharmacology

   Karthika, M and Devi, K G

Background : Hemoglobinopathies are the world wide prevalent monogenic genetic disorder affecting the structure, function, or production of hemoglobin with variable geographic distribution. In the southeast asia and Indian subcontinent, this has been considered as common disorder of blood posing a major genetic and public health problem. Objectives : To analyse the hemoglobin variants in Northeast India Materials and methods : This

is a Cross Sectional study conducted in the Department Of Physiology, Department Of Pathology, RIMS between Jan 2014-Feb 2015. A total of 100 from Northeast India were included in the study. Interlab Genio Instrument For Alkali and acid Hemoglobin Electrophoresis was used. Data Entry And Analysis Was Done Using SPSS Version-16. Approval Was Taken From The Rims Institutional Ethics Committee. Results : Among 100 of population surveyed 11% of the study population shows the presence of abnormal hemoglobin. 5% were found to be beta thalassaemia carrier, 4% HbE trait and 2% Sickle cell trait. Conclusion : High prevalence of hemoglobinopathies where Beta thalassaemia in heterozygous state occurred more frequent than other hemoglobinopathies. The study concludes that it is important to explore the hemoglobin variants in Northeast India so that the carriers can be detected and the serious damage to the future generation can be prevented.

6. **Alpha-thalassemia protects against severity of P. Falciparum malaria in Eastern India: A hospital based study**

   2014

   Indian Journal of Hematology and Blood Transfusion

   Purohit, P and Patel, D K and Patel, S and Mohanty, P K and Dehury, S and Meher, S and Das, K

Summary: The prevalence of alpha-thalassemia in patient with P. falciparum malaria was found to be 32.3 % and protect against severity of the disease manifestation. Introduction: Malaria is an important public health problem in Odisha. Alpha-thalassemia has been hypothesized to prevent against severe malaria. The prevalence of alpha-thalassemia in this area has found to be â˜¼ 50 %. Materials and Methods: Ninety six adult patients with P. falciparum malaria admitted in the Department of Medicine, were analyzed for alphathalassemia at Sickle Cell Clinic and Molecular Biology Laboratory, V.S.S. Medical College, Burla, Odisha. Alpha-thalassemia was analyzed by Multiplex PCR. On the basis of alpha-thalassemia, 96 patients were divided into two groups. Group-1: Patients without alpha-thalassemia and Group-2: Patients with alpha-thalassemia (both heterozygous (-Î± /Î± Î±) and homozygous (-Î± /-Î±) alpha-thalassemia). Results: The prevalence of alpha-thalassemia was found to be 32.3 % both in heterozygous (19.8 %) and homozygous (12.5 %) state. Both 3.7 and 4.2 kb deletional alpha-thalassemia were found with a gene frequency of 0.203 and 0.020, respectively. Hemoglobin and WBC level were significantly high where as MCV, MCH, serum-bilirubin and serum-creatinine were significantly low in Group-2 compared to Group-1. Clinical evaluation revealed that patients in Group-2 had a lower degree of having anemia, acute renal failure, jaundice and death compared to patients in Group-1. Conclusion: Presence of alphathalassemia in patients with P. falciparum malaria has a protective effect on the severity of the disease manifestation. High incidence of alpha-thalassemia in this area probably reflects a selective advantage of these people against death from P. falciparum malaria.

7. **Hepatobiliary manifestation in sickle cell disease (SCD) patients of Kerala**

   2019

   Journal of Gastroenterology and Hepatology

   Muhammad, S and Ramachandran, T

Background: There is lack of studies in Kerala on hepatobiliary manifestation in sickle cell disease despite many patients with SCD are being admitted yearly. Methods: Demographic and relevant clinical information, liver function test results, USG abdomen were collected from SCD patients admitted. CECT abdomen, MRI liver and fibroscan were done in indicated patients. All patients were followed up on 6th month. Results: 63 patients with SCD admitted at Calicut Medical College for various symptoms were evaluated. 26(41%) patients had jaundice on presentation, 11(17%) had abdominal pain, 2(3.2%) had abdominal distension, 1 (1.6%) had pruritus, 1(1.6%) had altered sensorium, 1 had hematemesis (1.65). Splenomegaly was present in 37(58%), hepatomegaly in 10(15%), ascites in 1(1.5%), altered sensorium in 2(3%). Conjugated hyperbilirubinemia was seen in 16 patients (25%). ALT more than ULN was seen 23(38%) of patients. ALP was >ULN in 13 patients (22%). USG abdomen was done in all patients 28(44%) patients had hepatomegaly. 1 (1.5%) patient had multiple cholangitic abscess in

liver. Gall stone was present in 21(33%) patients and 3(4.5%) patient had CBD calculi. Follow up showed significant fibrosis in 40% patient with acute hepatic manifestations. Conclusion: 29(46%) patients had hepatobiliary manifestations. These were acute hepatic crisis in 4(13.7%), acute hepatic sequestration in 3(10.3%), fatty liver in 4(13.7%), sickle cell cholangiopathy in 2 (6.8%), cirrhosis liver with ACLF in 1(3.4%), acute intrahepatic cholestasis in 1(3.4%), choledocholithisis with cholangitis in 1(3.4%), acute cholecystitis in 1(3.4%), acute hepatitis of unknown etiology in 1(3.4%) and cholelithiais in 21 (72%). The risk factors for hepatobiliary manifastations are age, male sex, history of sickle cell crisis, low haemoglobin. Hepatobiliary manifestations are associated with increased risk for hospital stay (p value <.01), hospital readmission(P-<0.01) surgery, development of fibrosis in 6 months (p value<0.0.1) and death.

8. **Patient and healthcare professional perceptions of sickle cell disease impact on daily life, symptom burden and treatment: Results from the international sickle cell world assessment survey (SWAY)**

   2020

   HemaSphere

   Trimnell, C and James, J and Andemariam, B and Inusa, B and El Rassi, F and Francis-Gibson, B and Nero, A and Minniti, C and Abboud, M R and Arlet, J.-B. and Colombatti, R and De Montalembert, M and Jain, S and Jastaniah, W and Nur, E and Pita, M and Ramscar, N and Bailey, T and Rajkovic-Hooley, O and Osunkwo, I

Background: Vaso-occlusive crises (VOCs) are the most common cause of hospitalization in sickle cell disease (SCD) and can cause severe pain, life-threatening complications and substantial emotional burden. Understanding patient (pt) perceptions of the impact of SCD and available treatments is important to identify unmet needs and tailor treatment to reduce disease burden. Healthcare professionals' (HCP) perceptions give insight into the evaluation of SCD. Aims: To investigate pt and HCP perceptions of SCD impact and treatment options. Methods: SWAY was a multi-country survey of unmatched SCD pts and HCPs developed by international SCD experts, pt advocacy groups and Novartis. Survey questions assessed perceptions of symptoms, impact, and treatment using a 7-point Likert severity scale; a score 5-7 indicated 'high severity/impact'. Results: 2145 SCD pts and 365 HCPs were surveyed from 16 countries across five continents. The mean pt age was 25y (standard deviation 12.9, range 6-75), 52% female. HCPs included primarily hematologists (41%), hematologist-oncologists (28%) and general practitioners (14%). The mean total SCD caseload was 430 pts per HCP, with a mean 76 pts in the past 12 months. The symptoms most frequently reported by HCPs as having a high impact on quality of life (QoL) were pain (acute, 88% and chronic, 84%), bone aches (76%), and fatigue (72%). In the pt survey, acute and chronic pain were not included in the symptom list and VOCs defined as 'severe pain crises' were assessed separately. Of the symptoms included, 65% of pts reported fatigue and 51% bone aches. Of the pts reporting these symptoms, 66% and 67% rated them as 'high severity'. Treatment goals were similar for HCPs and pts; improving QoL (64% vs 55%), preventing worsening of SCD (32% vs 43%), reducing VOCs (43% vs 30%). The statements 'Frustration with symptoms' and 'Worry about SCD worsening' were ranked 'high impact' by most HCPs (82% and 78%) and pts (58% for both statements) but a greater proportion of HCPs reported high emotional impact compared with pts for each statement (Figure). A greater proportion of HCPs compared with pts also considered SCD to have a high impact on household activities such as housework and childcare (72% of HCPs vs 38% of pts). Similarly, 71% HCPs vs 41% pts reported a high impact on family or social life. This difference was also seen with physical activity; 51% and 84% of HCPs reported that patients avoid mild and intense physical activity, respectively, whereas pts reported this to be 26% and 62%. Only 49% of HCPs reported high satisfaction with treatment options with limited options the main reason for dissatisfaction (90%). Pts were asked if satisfied with their treatment with only 66% reporting high satisfaction. 72% agreed with the statement 'I wish there was an alternative treatment to my current pain medication'. Summary/Conclusion: Results show that a lower proportion of pts compared with HCPs report a high impact on QoL of SCD, although results are confounded by the unmatched cohorts. One explanation is that pts may perceive a reduced level of emotional and physical wellbeing as normal, considering SCD is present from birth. Alternative explanations include a lack of discussion between pts and HCPs or bias caused by HCPs being more likely to see patients on days when they are unwell. Phenotype heterogeneity is another explanation; a subset of pts may have substantial unmet needs and others a lower disease burden. Both pts and HCPs have treatment concerns, indicating a need for additional and alternative treatments.

9. **Severe Malnutrition and Anemia Are Associated with Severe COVID in Infants**

   2021

   Journal of Tropical Pediatrics

   Kulkarni, R and Rajput, U and Dawre, R and Sonkawade, N and Pawar, S and Sonteke, S and Varvatte, B and Aathira, K C and Gadekar, K and Varma, S and Nakate, L and Kagal, A and Kinikar, A

Background: COVID-19 is uncommon and less severe in children than adults. It is thought that infants may be at higher risk for severe disease than older children. There is a paucity of literature on infants with COVID, particularly those with severe disease. Objective: We describe demographic, epidemiologic, clinical, radiological, laboratory features and outcomes of infants with confirmed SARS-CoV-2 infection admitted to a tertiary care teaching hospital in Pune, India Methodology: Infants who tested positive for SARS-CoV-2 and were admitted between 1 April 2020 and 7 August 2020 were included in the study. Results: A total of 13 infants were admitted during the study period. The median age was 8 months (IQR 6) and nine were male. Common presenting features were fever (n = 8, 62%), poor feeding, irritability, and runny nose (n = 3, 23%). Comorbidities noted were severe acute malnutrition (SAM) in three cases (23%) and nutritional megaloblastic anemia, iron deficiency anemia, sickle thalassemia and renal calculi in one case (8%) each. There was a history of low birth weight in two cases (15%). Pallor was noted in three cases (23%), SAM in three cases (23%) and tachypnea and respiratory distress in four cases (30%). Severe anemia, thrombocytopenia, elevated ferritin, abnormal procalcitonin, abnormal C Reactive Protein and deranged D-dimer was noted in three cases (23%) each. Neutrophil-lymphocyte ratio was normal in all cases. Three infants (43%) had evidence of pneumonia on the chest radiograph, of which one had adult respiratory distress syndrome (ARDS) like pattern, one infant had cardiomegaly and perihilar infiltrates. Hydroxychloroquine and azithromycin were given to five patients (38%), Intravenous Immunoglobulin and methylprednisolone were administered to one patient (8%). One infant died of ARDS with multi-organ dysfunction with refractory shock and hemophagocytic lymphohistiocytosis. Conclusion: SAM and anemia may be associated with severe COVID in infants.

10. **Relative incidence of different thalassaemias and haemoglobinopathies in South Bengal**

    2009

    Journal of the Indian Medical Association

    Manna, A K and Dutta, S K and Chatterjee, A

Thalassaemia is a common congenital abnormality throughout the world and beta-thalassaemia and HbE abnormality are two common haemoglobin disorders in West Bengal of India. There is inadequate study of these disorders in and around Calcutta, which is the most populated area in West Bengal. The present study showed 74.85% normal chromatogram on high performance liquid chromatography; 9.16% showed symptomatic patients of which commonest was E beta-thalassaemia followed by beta-thalassaemia. Asymptomatic patients with abnormal haemoglobin was found in 15.99% of which beta-thalassaemia minor was the commonest. Other studies in and around Calcutta also showed similar results. Studies involving population of 24 Paraganas of West Bengal showed less percentage of carrier state than the present study. This signifies the increased awareness of the urban and semi-urban population than the rural population regarding these congenital diseases. Only screening procedure can prevent spread of these diseases amongst general population.

11. **Prevalence of sickling in a selected spot of Rajnandgaon district (Chhattisarh, India) and its association with prevalence of plasmodium falciparum**

    2011

    HUGO Journal

    Anil, K and Seema, T and Rakesh, D

Sickle cell disease is a blood disorder resulting from inheritance of abnormal gene from parents. It is caused due to mutation in the-globin gene. Sickle cell disease is wide spread in Central India. Present study was under taken to study the prevalence of the disorder in Rajnandgaon district of Central India. A random sampling of 1749 people, was done to test sickling problem. By slide test method 71 people were found sickled positive. Further electrophoresis test was performed for all 71 of which 24 were found homozygous (HbSS) and 47 were found heterozygous (HbAS) positive. Beside above analysis, chloroquine prophylaxis associated with high prevalence of Plasmodium falciparum Pfcrt K76T mutation in people (n=26) with sickle cell disease was also analyzed. The genotype of the subject was screened using hemoglobin electrophoresis system and the P. falciparum Pfcrt genotyping was carried out using PCR-restriction fragment length polymorphism (RFLP). The prevalence rate of Pfcrt K76T mutant gene was proportionately found higher in the hemoglobin SS (n=9, m=6, r=0.66) genotype individuals than the hemoglobin AS (n=17, m= 9, r=0.52) and AA (n=32, m= 12, r=0.37).

12. **Prevalence of heamoglobin variants, ABO and rhesus blood groups in Northern Uttar Pradesh, India**

    2013

    Biomedical Research (India)

    Verma, P and Singh, S and Krishna, A and Ali, W and Tiwari, S

Hemoglobin variants are mutant forms of hemoglobin in a population, caused by variations in genetics. It's occurring when there are genetic changes in specific genes, or globins that cause changes or alterations in the amino acid. Hemoglobin variants, ABO and Rhesus blood groups are known to vary from one population to another. Thus, there is need to elucidate the frequency of these indices in Northern U.P., India. The result would serve as a platform for instituting genetic counseling services with a view to reduce haemoglobinopathies. Total 933 subjects aged 18 - 55 years were screened, 636 (68.17%) males and 297 (31.83%) females. Result of present study showed 12.01% prevalence of haemoglobinopathies. Out of total haemoglobinopathies screened subject, Î²-thalassemia in heterozygous state was found more frequent (5.04%) than Î²-thalassemia in homozygous state (0.43%). Other haemoglobinopathies followed by HbAE 3.32%, HbAS 0.86%, HbE-Î² 1.82% and HbS-Î² 0.54%. The frequencies with respect to ABO systems had been shown as O > B > A > AB. The distribution of Blood groups with 97.43% Rhesus positive (Rh+) out of which, O+(36.55%), B+ (35.78%), A+(18.97%), AB+ (6.11%) found respectively. In our study the Blood group O+ (36.55%), was most frequent but the higher prevalence haemoglobinopathies was found in Blood group A+ (33.93).

13. **Prevelance of haemoglobinophaties in Gujarat, India: A cross-sectional study**

    2009

    Internet Journal of Hematology

    Patel, J and Patel, A and Patel, J and Kaur, A and Patel, V

Various haemoglobinopathies are major public health problem in Gujarat, a state located in the western part of India. The data pertaining to their occurrence and prevalence in the state of Gujarat are scarce and hence it was considered worthwhile to study the burden of haemoglobinopathies in Gujarat, India. A retrospective analysis of blood samples of 428 cases referred to the pathology laboratory from various private practitioners/Government hospitals for the workup of anemia or other blood related disorders was done by Bio-Rad D-10 instrument. 153 (35.7%) patients out of 428 had haemoglobinopathies. Thalassaemia minor (70 cases, 16.35%), thalassaemia major (32 cases, 7.48%), sickle cell disease (22 cases, 5.14%) and sickle cell trait (12 cases, 2.8%) were most common haemoglobinopathies. Less prevalent haemoglobinopathies were sickle-Î²-thalassaemia, Î±,Î²-thalassaemia heterozygote, Hb D trait, Hb E trait, Hb E-thalassaemia, Hb D disease, Hb E disease and sickle D disease. Our study indicates that almost all the common haemoglobinopathies are prevalent in Gujarat but sickle cell trait/ anemia and Î² thalassaemia are very common.

14. Splenic infarct as an harbinger for sickle cell traits in high altitude

2017

Blood

Nair, V and Yanamandra, U and Kapoor, R and Kumar, R and Ranjan Das, S and Sharma, A and Jasjit, S and Pramanik, S and Sharma, S and Verma, T

Background: Sickle cell trait (SCT) is a common genetic abnormality in the so called 'Sickle belts' in India. Splenic infarction often brings to medical attention an underlying SCT, when appropriately looked for. The hypoxic environment of high-altitude area (HAA) is conducive for developing a splenic infarct in an SCT individual. Soldiers get frequently exposed to extreme altitudes. Aim & Objective: The objectives of the study were (a) To identify the incidence and etiology of splenic infarcts in HAA. (b) To identify the predisposing factors for splenic infarct with sickle cell trait from all patients managed at a tertiary care hospital at sea level. Methodology: The study was done in two phases. Phase I of the study was conducted at an high altitude (HA) secondary care hospital. All patients admitted with splenic infarct (n-82) to this hospital over a period of 1.5y were evaluated for limited thrombophilia states (FVL mutation, PNH, Polycythemia, MTHFR mutation, JAK2 mutation) and sickle cell trait. Also, these patients were evaluated for portal vein thrombosis or concomitant thrombosis of any other sites. Phase II of the study was conducted at a tertiary care referral center of the armed forces, where all the patients with concomitant sickle cell trait and splenic infarct were evaluated for precipitating causes over a period of 04y (n-51). Results: A total of 82 patients were admitted with splenic infarct to the HA secondary care hospital during the study period. The median age of the population was 28.4y (range: 23-42y) and all were males. They constituted 38.31% of all cases of thrombosis (214) admissions at HA in the given study period. They were second only to DVT (112, 52.33%) in the incidence of HA associated thrombosis, which were followed by CVT (16, 7.47%) and PTE (14, 6.54%) (Patients had variable combinations of DVT/ PTE/ CVT/ Splenic infarcts). Patients of splenic infarcts initially presented to surgeon in 85.3% instances (n-70) with pain abdomen (88%, n-72) or pleuritic pain (33%, n-27). Concurrent thrombosis at other sites were present in 33% (n-27) of the patients, of which 25.6% (n-21) had thrombosis of spleno-portal axis. High altitude illnesses were present in only 7.3% (n-6) of the patients. The mean duration to occurrence of the splenic infarct was 124.2 days (SD-31.8) after arrival to HA, but was less than 5.4 days (SD - 2.1) in patients with sickle cell trait ($p<0.01$). The etiology was mostly idiopathic (64.6%, n-53) followed by sickle cell trait in 24.4% (n-20) and other thrombophilia states in 10.9% (n-9) cases. Among the secondary causes, sickle cell trait was the commonest cause. Among the idiopathic cases few might have been secondary to protein C/ S or Antithrombin III deficiency which could not be evaluated during the acute phase. In patients with sickle cell trait, sickling at the time of splenic infarct at HA was seen in only 55% (n-11) though expected to be 100%. Family history was present in only 5% (n-1) of the patients with sickle cell trait of any sickling syndrome. In phase II of the study, a total of 51 cases of sickle cell trait with splenic infarcts were admitted in the study period, who were evaluated. The median age of the study population was 29.6y (range: 21-48y). Of these, 82.4% (n-42) patients had developed the splenic infarct on exposure to HAA. Clinically splenomegaly was seen in 25.5% (n-13) patients with splenic infarct at presentation. The mean HbS was 37.34% in the SCT patients. A thrombus in the spleno-portal axis was demonstrated in 17.6% (n-9) of cases. The splenic rupture was a rare event, seen in only one patient. Splenectomy was done in only one patient due to non-resolving abscess. Of these patients 09 patients had sickle cell syndrome on exposure to severe exertion (n-8) / fever (n-1) at plains. Conclusion: It is important to test for sickle cell trait in these otherwise healthy soldiers who develop splenic infarct at HA. The clinical importance of otherwise benign sickle cell trait in the form of splenic infarct by HA exposure or severe exertion is elucidated by this study.

15. Changing epidemiology of maternal mortality in rural India: Time to reset strategies for MDG-5

2014

Tropical Medicine and International Health

Shah, P and Shah, S and Kutty, R V and Modi, D

Objective: To understand changes in epidemiology of maternal mortality in rural India in the context of increasing institutional deliveries and implementation of community-based interventions that can inform policies to reach MDG-5. Methods: This study is a secondary analysis of prospectively collected community-based data of every pregnancy and its outcomes from 2002 to 2011 in a rural, tribal area of Gujarat, India as part of safe-motherhood programme implemented by voluntary organisation, SEWA Rural. The programme consisted of community-based interventions supported by a first referral unit, and promotion of institutional deliveries. For every maternal death, a verbal autopsy was conducted. The incidence rates for maternal mortality according to place, cause and timing of maternal deaths in relation to pregnancy were computed. Annual incidence rate ratios (IRR) and 95% confidence intervals, adjusted for caste and maternal education, were estimated using Poisson regression to test for linear trend in reduction in mortality during the study period. Results: Thirty-two thousand eight hundred and ninety-three pregnancies, 29 817 live births and 80 maternal deaths were recorded. Maternal mortality ratio improved from 607 (19 deaths) in 2002-2003 to 161 (five deaths) in 2010-2011. The institutional delivery rate increased from 23% to 65%. The trend of falling maternal deaths was significant over time, with an annual reduction of 17% (adjusted IRR 0.83 CI 0.75-0.91, P-value <0.001). There were significant reductions in adjusted incidence rate of maternal deaths due to direct causes, during intrapartum and post-partum periods, and those which occurred at home. However, reductions in incidence of maternal deaths due to indirect causes, at hospital and during antepartum period were not statistically significant. Most maternal deaths are now occurring at hospitals and due to indirect causes. Conclusion: Gains in institutional deliveries and community-based interventions resulting in fewer maternal deaths due to direct causes should be maintained. However, it would be essential to now prioritise management of indirect causes of maternal mortality during pregnancy at community and hospitals for further reduction in maternal deaths to achieve MDG-5. Â© 2014 John Wiley & Sons Ltd.

16. **Red cell alloimmunization in multitransfused patients at a tertiary care teaching hospital**

    2020

    Indian Journal of Hematology and Blood Transfusion

    Sinha, S K and Kumar, S

Aims & Objectives: Red blood cell alloimmunization is an immune competent host evoked response against the unknown RBCs antigens not present in the body. It occurs mostly after repeated blood transfusion or in pregnancy. Aim of this study to determine the seroprevelance and specificity of RBC antibodies in multitransfused patients, in whom the risk of alloimmunization is high. Patients/Materials & Methods: This study was conducted in Department of Pathology and Blood bank of Sir Sunder Lal Hospital, Institute of Medical Science, Banaras Hindu University, Varanasi. Blood was drawn from the patient of thalassemia major,sickle cell disease, haemat-oncology cases,chronic renal failure with haemodialysis, Pregnancy with complications and bad obstetric history, transfusion dependent oncology cases,anemia,bleeding disorder, Rh incompatible cases, and rest all the cases those requiring multiple blood and its component transfusion. The serum was used for antibody screening and identification test. Three cell antibody screening was performed using antihuman globulin gel cards(ID-Card LISS/ Coombs) and three cell panel (ID-Diacell I,II,III BioRad). Those with positive antibody screening were analyzed further for antibody identification test using 11 cell panel(Set ID-Dia Panel BioRad). Results: Overall prevalance of RBC alloantibodies was 4%. Of the 15 specific type of alloantibody identified, most (53.3%) belonged to Rh blood group system, followed by Kell blood group(20%), bombay blood group(13.3%),and Duffy blood group(6.6%). Discussion & Conclusion: Red cell alloimmunization in multiple transfused patients should not be ignored. To prevent the risk ofhemolytic reactions and delay the reaction, regular antibody screening and its identification should be done in set interval of time after transfusion. Especially in patient who required long term blood transfusion and in those at higher risk of alloimmunization. RBC transfusion is a lifesaving practice, which explains why all these procedures results into safe and sufficient quality of blood supply.

17. **Hematological indices and hemoglobin high-pressure liquid chromatography for diagnosis of hemoglobinopathies in a secondary care center in North-East India**

2021

International Medicine

Mishra, M N and Sangma, B and George, D M and John, L and George, K C

Background: Hemoglobinopathies occur globally and are often presented with anemia. This study was performed in a secondary care center in Sonitpur District, Assam, to study the usefulness of hematological indices and hemoglobin High-Pressure Liquid Chromatography (HPLC) for characterization of hemoglobinopathies and to quantify the prevalence and types of anemia in a resourcepoor setting of North-East India. Methods: Data of 9936 hemoglobin estimations and 708 peripheral blood smear examinations performed over a year were retrieved. Complete blood count for 170 patients was performed by XS 800i Five-Part Sysmex Cell Counter whereas hemoglobin (Hb) HPLC was outsourced. Serum iron estimation was done for 100 samples by dry chemistry and serum ferritin assay was tested by direct chemiluminescence for 13 patients. The number of hospital visits, hospitalization duration, blood transfusions, demographic profile, and unusual features in some patients was recorded. Results: Anemia (Hb < 11.0 g/dl) was present in 79.6% of 9936 samples tested. Microcytic hypochromic anemia was present in 278/534 (52%) patients. The mean age of 170 subjects was 15.4 years (3 months - 56 years) with a slight female preponderance 87/51.2%. Erythrocytosis was observed in 32/18.8% of samples, of which 18 were females. Microcytosis and low mean corpuscular hemoglobin (MCH) were observed in 143 (84.1%) and 153 (90%) samples, respectively. The number and percentage of conditions identified by HPLC are no abnormality in 53 (31.2%), hemoglobin E disease 31 (18.2%), hemoglobin E trait 25 (14.7%), Î²-thalassemia minor 11 (6.5%), Î²-thalassemia major 4 (2.4%), compound hemoglobinopathy 15 (8.8%), sickle cell trait 12 (7%) and sickle cell disease 8 (4.7%), and inconclusive in 11 (6.5 %) patients. Serum iron was low in 39 (34.5%), normal in 65 (57.5%), and high in 9 (8%) of the 113 subjects tested. Conclusions: Prevalence of anemia and hemoglobin E abnormality was high with unexpected severe anemia in some heterozygotes for HbE, HbS, and Î²-thalassemia. Hemoglobin HPLC was useful in arriving at a presumptive diagnosis and must be used as a frontline investigation even in resource-poor settings.

18. **Genetic mutation at 567C/G of Bone Morphogenetic Psrotein-6. reveals no significant involvement of pathological progression in sickle-cell disease with orthopedic complications but strongly associated with increased ldh and uric acid level in indian patient**

2014

American Journal of Biochemistry and Biotechnology

Abhishek, K and Sohail, M and Zaidi, A and Anwar, S and Roy, V P and Sharma, A K and Adak, T and Raziuddin, M

Background and objectives: Sickle cell disease has numerous consequences; one of the most characteristic is orthopedic complications. Bone Morphogenetic Proteins (BMPs) are involved in the various orthopedic complications and play important role in bone physiology influencing bone growth, turnover, bone formation and cartilage induction. We investigate a possible association of sickle cell disease with orthopedic disorders through BMP6 gene polymorphism. Methods: Among the population studied in Chhattisgarh and Jharkhand states (a total of 200 cases and 172 control groups), the association was examined between SNP 567C/G of BMP6 and orthopedic complications in sickling patients by employing PCR-RFLP and biochemical analysis. Results: 567C/G SNP has not been implicated in disease and doesn't increase the risk (OR = 1.27. OR = 0.85). We observed no significant association between the 567C/G polymorphism and case group in the studied population (P = 0.64, P = 0.91, respectively). However, significantly elevated Uric Acid (UA) level (P = 0.0001, P = 0.0001, P = 0.0001 and P = 0.0001, P = 0.0001, P = 0.0001 respectively) and Lactate Dehydrogenase (LDH) level (P = 0.0001, P = 0.0001, P = 0.0001 and P = 0.0001, P = 0.0001, P = 0.0001 respectively) in GG, CG and CC in case group as compared to control group among the studied population. Interpretation and Conclusions: 567C/G polymorphism in BMP6 gene is not associated with case group and in view of present observation, we suggest that evaluation of

LDH and UA level and its association with polymorphisms in the BMP6 may be considered as a reliable molecular and biochemical markers possesses promising rational for diagnostic potential in clinical cases. Â© 2014 Science Publication.

19. **Undiagnosed haemoglobinopathies among pregnant women attending antenatal care clinics in Pune, India**

    2021

    Journal of Community Genetics

    Dharmarajan, S and Pawar, A and Bhide, P and Kar, A

Pregnant women with iron deficiency and those who are carriers of haemoglobinopathies present with anaemia of varying severity. There is no antenatal screening for haemoglobinopathies in India. The objective of this study was to determine the prevalence of undiagnosed haemoglobinopathy carriers in a random sample of pregnant women attending antenatal care clinics in Pune city, India. Biobanked DNA of 360 randomly selected pregnant women was genotyped for six common mutations and two common haemoglobin variants, HbS and HbE. Odds ratios (OR) with 95% confidence intervals were computed to determine association of carrier status with socio-demographic, haematological and clinical characteristics. The prevalence of undiagnosed haemoglobinopathy carriers was 6.3% (95% CI 4.2â€“9.4%) of which 3.3% (95% CI 1.9â€“5.7%) were beta thalassaemia carriers. There was an increased odds that beta thalassaemia carriers had moderate anaemia (OR 10.59, 95% CI 1.15â€“96.90). This study reveals the high prevalence of undiagnosed haemoglobinopathy carriers among pregnant women, indicating the need to immediately implement carrier screening and genetic counselling services across the country.

20. **Prevalence of hemolytic anemia and hemoglobinopathies among the pregnant women attending a tertiary hospital in Central India**

    2015

    Thalassemia Reports

    Balgir, R S

Anemia in pregnancy is one of the causes of maternal morbidity and, maternal and fetal mortality in India. Hemoglobin transports oxygen to different parts of the body. Any defect in hemoglobin structure leads to its adverse functions. Screening of pregnant women for hemoglobinopahties helps in early intervention for reducing morbidity and mortality. Although the prevalence of hemoglobinopathies especially of the sickle cell disorders is high in Madhya Pradesh but any study on pregnant women is lacking. This study had set the objectives to find the prevalence of anemia and hemoglobin disorders in pregnant women, and to determine the health status through hematological indices profile in central India. Hospital based a cross-sectional study showed 12.26% prevalence of hemoglobinopathies among 416 pregnant women, the sickle cell trait being 7.45%, followed by b-thalassemia trait (2.89%), hemoglobin E trait (0.24%), and sickle cell disease (1.68%). About 88% of the pregnant women were found free of hemoglobinopathies. Of the 9.13% pregnant women included in the study were suffering from sickle cell disorders. However, the overall 47.11% anemia was observed in pregnant women, ranging in between 45% to 66% and seemed to show a reduction in anemia after nutritional supplementations and improvement in maternal health care at antenatal check up due to accessibility to medical health facilities. A comparison of hematological indices of pregnant women afflicted with and without sickle cell disorders have revealed much reduced hemoglobin level, red blood cells count, mean corpuscular volume, hematocrit, and mean corpuscular hemoglobin; and raised leucocytosis in sickle cell disorder cases than among the normal pregnant women. A more vigorous and realistic campaign of prophylactic regime of supplementations for these pregnant women and child health care is suggested.

21. **Sickle cell anaemia during infancy**

    1980

    Indian Pediatrics

    Samel, G C

The incidence of sickle-cell disorder in Western Orissa was found to be 6.75%. Of this (17 cases), 0.36% were infants under 1 yr of age suffering from homozygous sickle-cell anaemia (SS). The chief clinical features were anaemia, splenomegaly, hepatomegaly, jaundice, abdominal tenderness and bone tenderness in 100, 100, 8.35, 58.82, 53.23 and 41.17%, respectively. Only 23.52 and 17.64% had hand-foot syndrome and bleeding episodes. All patients had anaemia with reduction of hemoglobin and TRBC. All the patients had raised reticulocyte count and foetal hemoglobin.

22. **Manual partial exchange transfusion a cost effective life saving intervention in sickle cell crisis: Single centre retrospective dataanalysis**

    2020

    Blood

    Bhatwadekar, S S and Vishwas Deshpande, S and Vikas Khadse, S and Shah, B and Desai, D and Jani, D and Vasoya, P and Lakhmapurkar, U and Shah, S and Shah, A J

Introduction: Sickle cell disease (SCD) poses a considerable health burden in lower middle income country (LMIC)like India. One ICMR survey reported about 20% of children with SCD died by the age of two yearsand 30% of children with SCD amongst the tribal community in India died before they reachedadulthood. Data on mortality rate in the adult population with SCD is sparse. Our centre data showsthat despite the availability of Hydroxyurea and supportive care, almost one-third of hospitalizedSickle Cell Crisis patients develop life threatening complications. Manual Partial ExchangeTransfusion is a cost-effective intervention to decrease mortality in Sickle Cell Crisis. But perhaps, itis an underutilized therapy. In India, the cost incurred for each session of exchange transfusion, ifdone by the RBC apheresis machine, is $420. Whereas Manual Exchange Transfusion costs only$70(including the cost of the central venous catheter) for the first session followed by $15 for eachsubsequent session. Aim: A single centre retrospective data analysis to evaluate the outcome of Sickle Cell Crisis patientsundergoing Manual Partial Exchange Transfusion during hospitalization. Material and Method: A total of 553 SCD patients on regular follow up at the Haemato Oncology Care Centre (HOCC) fromJuly 2012 to July 2020 were evaluated.169 patients were hospitalized for treatment of Sickle Cell Crisisat the Bhailal Amin General Hospital and Sterling Hospital Vadodara. The data was retrieved after theIRB/Apex committee approvals for retrospective analysis. The indication for exchange transfusionwas Acute Chest Syndrome 19(35%), Hepatic cell crisis 11(20%), Vaso Occlusive Crisis notresponding to the conservative line of therapy in 48 hours of treatment 11(20%), CerebrovascularAccident (CVA) 5 (9%), Avascular Necrosis of Femur with excruciating pain 3 (6%), ComplicatedDengue with Multi-organ failure 3 (6 %), Priapism 1 (2%) and Splenic Sequestration 1 (2%). Centralvenous access was secured with a central venous catheter or dialysis catheter. Simple packed cellvolume was transfused to 11(20%) patients and 5(9%) patients received platelet transfusion. The cut-off values for HB and Platelet count were 8 gm% and 50000/cumm, respectively at the time of theManual Partial Exchange Transfusion procedure. Blood volume withdrawn was 5 to 10 ml /kg,followed by an equal volume of packed cell volume transfusion at every session. The procedure wasrepeated every 12 hr or 24 hr depending on the clinical condition of the patient. HbS value wasreassessed post 4 sessions with repeat testing done after 2 to 4 sessions if the observed HbS valuewas more than 30% or more than 10% (for CVA) after 4 sessions. The endpoint was clinical recovery with HbS less than 30% or no clinical recovery despite the achievement of HbS less than 10%. InCVA the endpoint was HBS less than 10%. Results: Manual Partial Exchange Transfusion was carried out in 54/169 (32 %) hospitalized patients. Themedian age was 25yrs (range 5 yrs to 69 yrs), with male predominance [Males 42(77%) and females12(23%)].Pre procedure HbF value was <10% in 13(24%), 10 to 20% in 23 (43%) and >20% in 18(33%).A total of 50 out of 54 (93%) patients recovered completely. 28 (52%) patients werehemodynamically stable with normal SPO2 on room air at the time of Manual Partial ExchangeTransfusion

with an average of 7 days of hospitalization. All of these patients recovered completely with less than 5 sessions of Manual Partial Exchange Transfusion. 26(49%) patients were critically illand had an average of 12 days of hospitalization. They were on Ventilator and Inotrope support at thetime of Manual Partial Exchange Transfusion. 14/26(54%) critically ill patients recovered completely with an average of 6 sessions of Manual Partial Exchange Transfusion. 12/26(46%) critically illpatients succumbed even though post exchange HBS value decreased to less than 10%. The overallmortality rate of SCD patients in this analysis was 12/553 (2.1%), significantly lower than what washistorically reported as 30% in the ICMR survey. Underlying Dengue viral infection associated with Multi-organ dysfunction and Fulminant hepatic failure were risk factors for mortality observed in ourstudy. Conclusion: Manual Partial Exchange Transfusion is highly effective in reducing mortality in Sickle Cell Crisis. It isfeasible and cost-effective in small centres lacking apheresis machine facility.

23. **Prevalence and determinants of anaemia and effect of different interventions amongst tea tribe adolescent girls living in Dibrugarh district of Assam**

    2015

    Clinical Epidemiology and Global Health

    Mahanta, T G and Mahanta, B N and Gogoi, P and Dixit, P and Joshi, V and Ghosh, S

Problem considered: Anaemia, associated with lower productivity and higher sickness rate and absenteeism. Adolescent health has inter-generational effect. Morbidity status during adolescent has implication on future safe motherhood, optimum growth and development of foetus and children. Aims: To assess, prevalence and determinants of anaemia and effect of different interventions amongst tea tribe adolescent girls. Methods: A community based intervention study was conducted covering 16 tea estates of Dibrugarh district, Assam. Variables includes socio-demographic, environmental, anthropometry, history of present and past illness, clinical examination and laboratory investigation including haemoglobin, serum ferritin, sickling test and routine stool examination. Interventions like weekly IFA supplementation, dietary diversification, health promotion by monthly NHED, cooking demonstration, cooking competition and kitchen garden promotion was done. SPSS and EpiInfo software, used to calculate of rates, ratios, chi-square test, Fisher Exact test. Results: Enrolments were 802, with mean age, 14.8 years. Anaemia prevalence was 96.3% with median serum ferritin, 22.9 ng/ml. Prevalence of sickle cell anaemia was, 12% and helminthiasis 84.20%. Health related complaints, significantly more frequent amongst older adolescents ($p < 0.000$). History of passage of worms (9.1%), night blindness (5.6%), weakness (62.1%), loss of appetite (37.5%), gum bleeding (23.6%), loose motion (13%), loss of weight (9.9%), menstrual problem (19.3%) were common. Following intervention mean haemoglobin difference was 1.48 g/dl with 13.5% difference in prevalence. Associated morbidities showed significant improvement following active intervention. Conclusions: High anaemia prevalence requires urgent attention to avoid preventable morbidities. Integrated different intervention implementation found effective in reducing the burden of anaemia and associated factor.

24. **Clinico-pathological co-relation of maternal death in rural areas of north Maharashtra**

    2014

    International Journal of Pharma and Bio Sciences

    Vasaikar, M S and Kanthikar, S N and Tambse, M P

To study pathogenesis & morphological changes in various organs with clinicopathological co-relations of maternal death in rural areas of North Maharashtra. To compare maternal deaths of metropolitan cities with rural areas. To evaluate several factors which are responsible for maternal death in rural areas. This was a retrospective study of 122 maternal deaths tissue received for histopathological examination over a span of 5 years (January 2008-December 2012), in government Medical college Dhule. The tissue was received from Jalgaon, Nashik, Nandurbar and Dhule districts. Ten cases were excluded from present study due to improper fixation, partial organs & ill preserved specimens. Hence 112 cases of maternal deaths were studied. Out of 112 cases, 57 cases (50.89%) died due to direct obstetric cause, 58 cases (47.32%) died due to indirect causes and in 2 cases the cause

was unknown. Anemia (27.67%), Pre-eclampsia/eclampsia (28%), were the main causes of death. In 10 cases vaso-oclussive crisis due to sickle cell anemia was responsible for death. Anemia is the main cause of death in rural places of North Maharashtra, while Pre eclampsia/eclampsia is the main cause in Metropolitans cities. Thus early marriage, lack of education, ignorance has led to unutilisation of antenatal care services.

25. Distribution pattern of HbS and Î²-globin gene haplotypes among koya dora tribe of Andhra Pradesh

2011

International Journal of Human Genetics

Uma Mahesh, K S S and Aggarwal, A and Vijaya Bhasker, M and Mukhopadhyay, R and Saraswathy, K N

Sickle cell disease is a hemoglobinopathy characterized by the production of abnormal hemoglobin, HbS (sickle cell hemoglobin). HbS gene is widely prevalent across Indian populations, especially among tribal populations. In the present study, Koya Dora tribal group of Andhra Pradesh was screened for HbS gene and also for the associated Î² globin haplotypes. Hb*S was found to be present in a high frequency (16.2%) in the studied population. and no HbS homozygous individual was found. Molecular screening was done for four sites namely, HincII-ÏˆÎ², HincII-3' ÏˆÎ², HinfI 5'Î² and HbA/S. All the sites were found to be polymorphic in the population. Arab-Indian haplotype was the most common haplotype associated with Hb*S among Koya Dora. Three atypical haplotypes, Senegal, Benin and Bantu were also observed, although in low frequencies. Â© Kamla-Raj 2011.

26. Transcranial Doppler study among children with sickle cell anaemia vs normal children

2012

Journal of Nepal Paediatric Society

Lakhkar, B B and Lakhkar, B N and Vaswani, P

Introduction: Role of transcranial Doppler in prevention of stroke in sickle cell children has been well appreciated. Studies are being done to develop the protocol in children. Since we don't find stroke very commonly in this part of the world, this study was done in order to see the prevalence of abnormal flow velocity in sickle children attending sickle cell clinic. The aims of this study were to measure mean flow velocity in different vessels in homozygous sickle cell patients using transcranial Doppler study, to compare the mean velocity in sickle children with age and sex matched controls and to correlate mean velocity with headache or stroke if any and also to correlate mean velocity with number of transfusions. Materials and Methods: The study was done in Paediatric wards. It was a prospective crosssectional comparative study. Twenty six children below 14yrs of age with homozygous sickle cell disease attending the Sickle cell clinic were selected as the cases. Forty cases of similar age and sex were recruited as normal control group. Transcranial Doppler was done in six different vessels in both the groups and mean flow velocity was measured. Mean flow velocity was correlated with symptoms and number of transfusions. Velocity was classified as normal (<170cm/sec), conditional (170-199cm/sec) or abnormal (>200cm/sec). Statistical analysis was done using SPSS 10 software. Results: In normal age and sex matched controls mean blood flow velocity was 50cm/sec where as in the cases of sickle cell disease was 180cm/sec. Maximum mean velocity was observed in middle and posterior cerebral artery. In two Sickle cell cases (8%) blood flow velocity was abnormal, these children had headache though received 5-10 transfusions/year. In only 4% sickle cell children flow velocity was normal and rest had conditional velocity. Among these children 39% received less than 5 and rest received 5-9 transfusions /yr and had no symptoms of stroke. Conclusions: Flow velocity measured by Transcranial Doppler is highest in middle cerebral artery and Posterior cerebral artery which appear to be the best arteries for this test in this region. Flow velocity was significantly high in children with sickle cell disease as compared to normal children. Prevalence of abnormal flow velocity in our children was 8% and children with abnormal mean flow velocity presented with headache.

27. Profile of infections in paediatric hematopoietic stem cell transplant patients: Experience from a tertiary care centre in india

2016

Pediatric Blood and Cancer

Thakkar, D and Misra, R and Rastogi, N and Kohli, S and Nivargi, S and Yadav, S P

Background/Objectives: Hematopoietic stem cell transplantation (HSCT) is the definitive treatment modality for several malignant, non-malignant and primary immunodeficiency conditions in children. Though the success rates are increasing in leaps and bounds, infections are still a major cause of morbidity & mortality in patients undergoing HSCT. Design/Methods: We retrospectively analysed the profile of infections in paediatric patients who underwent HSCT at our centre from February2012 to December2015. Results: 53 patients underwent 61 HSCTs between February2012 to December2015 (9autologous and 52allogenic). M:F ratio 2.53:1 and average age 7.74years(range:5months- 22years). Graft source: bone marrow(BM):11/61(18.1%), G-CSF mobilized peripheral blood stem cells(PBSC)-41/61(67.2%), BM+PBSC-8/61(13.2%), umbilical cord blood- 1/61(1.6%). Indications for BMT: thalassaemia major(24.6%), sickle cell anemia(9.8%), severe acquired aplastic anemia(5%), congenital marrow failure(9.8%), primary immunodeficiency(14.7%), relapsed ALL(8.2%), CML(3.3%), MDS(3.3%), relapsed/refractory solid tumors (6.5%), relapsed/refractory neuroblastoma stage4(11.6%), Refractory NHL (1.6%), others (Epidermolysis bullosa dystrophica) (1.6%). Patients received prophylactic antifungal, antiviral and prophylaxis against Pneumocystis jiroveci. There were 53 documented infections in 61 transplants during and post HSCT;spectrum:34bacterial (5ESBL,10Klebsiella pneumoniae, 1Pseudomonas aeruginosa, 4Acinetobacter boumani, 7MRSA, 2Enterococcus faecalis,1Enterococcus faecium,1Stenotrophomans maltophilia,1CONS, 1Morganella morganii, 1Edwardsiella tarda), 14viral(7CMV,1EBV, 2BKV, 1Adenovirus, 1JC virus, 2Varicella), 3fungal(1Aspergilus, 1Candida tropicalis, 1Candida dubiliniensis) and 2BCGiosis. Distribution of occurrence of infections: 29-pre-engraftment, 20-post-engraftment upto D+100 postHSCT and 4-postD+100 of HSCT. Median time of occurrence of infection:10days postHSCT(rangeD-9toD+341) and mean time of Neutrophil engraftment:15.5days postHSCT(range9-26days) (9-non-engraftment,1-engraftment pending,1-rejection postengraftment). Mortality attributable to infection occurred in 8/61(13.1%). Conclusion: Infections in HSCT setup contribute to significant morbidity & mortality. Preventive & pre-emptive strategies should be sought for and applied wherever feasible to reduce the frequency of infections and improving outcomes for these patients.

28. Clinical and molecular characterization of Î²S and GÎ³(AÎ³Î´Î²)0-thalassemia in eastern India

2010

Hemoglobin

Patel, D K and Patel, M and Mashon, R S and Patel, S and Dash, P M and Das, B S

Fetal hemoglobin (Hb F) is the most studied modifier of sickle cell disease. Coinheritance of high Hb F determinants such as Î´Î²- thalassemia (Î´Î²-thal) and hereditary persistence of fetal hemoglobin (HPFH) can contribute to raised Hb F concentration in these patients. One hundred and seventy-six cases of sickle cell disease with high Hb F were screened for the presence of the Asian Indian deletion-inversion GÎ³(AÎ³Î´Î²)0-thal and HPFH-3 (Indian, 48.5 kb) disorders. Three cases from two unrelated families were found to have sickle cell disease and the (AÎ³Î´Î²) 0-thal genotype. Three other members had heterozygous GÎ³(AÎ³Î´Î²)0-thal. None had HPFH-3. Despite very high Hb F concentrations and linkage of the Î²S gene to Asian haplotypes, the compound heterozygotes had severe clinical presentation, possibly because of heterocellular distribution of Hb F. In conclusion, these high Hb F determinants are not common causes of high Hb F in Indian sickle cell disease patients. Â© 2010 Informa Healthcare USA, Inc.

29. Cholelithiasis in sickle cell disease

2019

Surgical Endoscopy

Mahajan, P

Vidarbha region of Central India hosts a large population suffering from sickle cell disease (SCD). Patients may be divided into 2 categories depending upon whether they harbour the sickle cell trait ' SA' pattern or ' SS' haemoglobinopathy. 25% of people suffering from either condition have gallstones due to haemolysis owing to polymerization of the HbS within the Red Blood Cells and sequestration of RBC's in the spleen. This leads to the formation of pigment stones in the gall bladder. Most of the patients have symptoms such as chronic right upper quadrant with intermittent pain acute exacerbations. Patients may be jaundiced due to the chronic haemolysis and also have bouts of obstructive jaundice from calculi that may intermittently slip into the common bile duct unless treated. Materials and Methods: 70 patients with cholelithiasis were studied over 5 years. 42 patients had sickle cell trait while 28 had 'SS' disease. The age range was between 15-40 years, with a mean age of 24 years. All the patients had symptoms of chronic cholecystitis. Mean bilirubin was 4.8 mg/DL Laparoscopy revealed characteristic features of chronic cholecystitis in all patients. The gall bladders were small, shrunken, thick walled and contained multiple pigmented calculi. The technical difficulties were as follows: 1) Very small size of gall bladder in all (100%) patients. 2) Chronic adhesions in the Calot's triangle in 75% of patients. 3) Thickened short contracted cystic duct in 90% of patients. 4) Impacted stones at the neck, causing difficulty in dissection (20%) 5) Intrahepatic gall bladder (25%) Results: Subtotal cholecystectomy had to be performed in 3 cases due to severe adhesions in the Calot's triangle. Post operative complications: Sickle cell crisis- acute chest syndrome, joint painsin 3 cases Extended hospital stay of over 5 days in 15 patients due to SCD related complications. Port infection in 4 patients. Mortality in 1 patient due to sickle cell crisis. Conclusion: 1) Laparoscopic cholecystectomy is technically difficult in patients with sickle cell conditions due to chronic inflammatory changes in the area. 2) Meticulous pre and post operative care is mandatory with adequate fluid infusions, good oxygenation, maintenance of OR temperature above 25 degrees Celsius, pre operative folic acid, sodium bicarbonate, hydroxyurea to prevent hypoxaemia, dehydration and hypothermia.

30. Clinico-hematological analysis of Hb variants and spectrum of hemoglobinopathies on HPLC: A 3 year study from a tertiary care centre of north india

2012

Indian Journal of Hematology and Blood Transfusion

Agarwal, P and Goyal, S and Mohanpuria, A and Kumar, V and Marwah, S and Nigam, A S and Buxi, G

Objective: To analyse and characterize various Hb variants and hemoglobinopathies using high performance liquid chromatography (HPLC). Methods: The present retrospective study was carried out at PGIMER, Dr. RML Hospital, by analysing the data obtained from September 2009 to August 2012. The clinical and haematological records of patients suspected of hemoglobinopathies were retrieved and studied with the HPLC pattern. Family studies carried out in indeterminate cases were also reviewed. Results: Abnormal haemoglobin fractions on HPLC were seen in 121 of the 1846 cases studied. Of these, beta thalassemia trait was the predominant abnormality with a total of 69 cases (57.02 %). HbS was the next most common Hb variant, observed in 18 cases (14.8 %). Of these, four cases were homozygous for sickle cell disease. Other hemoglobins observed were Hb D Punjab (7 cases; 5.78 %), alpha thal (7 cases; 5.78 %) and Hb E (5 cases; 4.13 %). Hb J Meerut, HPFH and combined Hb E/beta thal inheritance had 3 cases each (i.e. 2.3 % each). 5 cases also showed peak in the C window. 2 cases (1.6 %) were each of Hb Q India, Hb Lepore trait and beta thal major. Conclusion: Our study highlights that high performance liquid chromatography (HPLC) is a simple yet rapid and reliable tool for the detection of haemoglobin variants.

31. **Cholelithiasis in thalassaemia major.**

    2002

    Journal of the Indian Medical Association

    Krishna, K K and Diwan, A G and Mitra, D K

The incidence of gall stones in thalassaemia is less than that in sickle cell anaemia or hereditary spherocytosis. With adequate blood transfusions, the incidence is as low as 2%. There are not many reports on cholelithiasis in thalassaemia. A case of 24-year-old female with thalassaemia major and gall stone is reported here.

32. **Outcome after second haploidentical stem cell transplant (HSCT) in pediatric patients-a single-center experience from India**

    2020

    Pediatric Blood and Cancer

    Bansal, M and Dua, V and Chakraborty, S and Sachdev, M and Hamal, S and Bhargava, R and Kumar, M

Background and Aims: Graft failure is a known complication of allogeneic HSCT. Poor tolerance to reconditioning and increased risk of infections lead to high mortality rates during second transplants. Here weshare our experience who underwent a second haploidentical transplant at our center. Methods:We chose Post-Transplant Cyclophosphamide (PTCY) based approach in 8 patients and CD34 stem cells (positive selection) in 1 patient. This was a retrospective single center study. Results: Total 9 patients underwent second haploidentical HSCT. Indications for first HSCT were CML with ALL blast crises (2), thalassemia major (2), relapsed AML (1), relapsed ALL (1), sickle cell anaemia (1), JMML (1) and aplastic anaemia (1). Of these, 3/9 (33.3%) patients had primary graft failure, 2/9 (22.2%) secondary graft rejection, 2/9 (22.2%) relapse of the primary disease, 1/9 (11.1%) poor graft function and 1/9 (11.1%) developed donor derived leukaemia. Second HSCT was done at a median time of 37 days (range 27 - 740 days). Stem cells were taken from same donor in 2 while 7 from alternate donor. Seven out of 9 patients (77.7%) engrafted at a median of 12 days (range 11 - 26 days) whereas 2/9 (22.2%) died before engraftment from pulmonary bleed and the other from primary graft failure. Out of the 7 patients who engrafted, 1 (14.2%) died of infection, 1 from veno-occlusive disease and 1 from acute Graft versus host disease (GvHD). Four patients (44.4%) are alive after salvage transplant at a median follow up of 456 days (range 48 - 1095 days). Acute GvHD developed in 4/7 (57.1%) patients. No chronic GvHD was noted. With stringent monitoring for CMV and pre-emptive therapy, none succumbed to CMV disease. Conclusions: In a resource constrained setting, where patients are not even going for 1st transplant, our small sample size shows that a second haploidentical transplant is a feasible option.

33. **Salmonella typhi causing hip arthritis with dislocation**

    2014

    Journal, Indian Academy of Clinical Medicine

    Gupta, V and Priyadarshi, A and Mehra, N and Yadav, T P and Dewan, V

Salmonella typhi is endemic in several parts of India causing enteric fever. Salmonella typhi septic arthritis in children without risk factors like sickle cell anaemia, systemic lupus erythematosis, immunodeficiency, or trauma to joint, etc., is uncommon. Here we report a child with Salmonella typhi septic arthritis who developed dislocation hip while on treatment. Clinical presentation and management of the same has been discussed.

34. Control of thalassemia in India

2014

Thalassemia Reports

Colah, R B and Gorakshakar, A

The Î²-thalassemias and sickle cell disorders pose a major health burden in the large and diverse Indian population. Education programs for awareness generation are being done by National Institutions, non-governmental organizations and Thalassemia Societies in different states. Several extensive epidemiological studies have shown that there are many non-tribal and tribal communities where the prevalence of Î²-thalassemia carriers is much higher (5.3 to 17.0%) than the average of 3 to 4% projected for the entire country. These variations have also been shown within small geographic regions in some states, emphasizing the need for micro mapping to estimate the true burden of disease. There are 10 to 12 centers where prenatal diagnosis for hemoglobinopathies is done and the Indian Council of Medical Research is establishing additional regional centers in states where they are most needed. Sixtyeight Î²-thalassemia mutations have been described so far among Indians and the knowledge on their prevalence and regional distribution has helped to undertake prenatal diagnosis in a cost effective way.

35. Haematological profile in patient of sickle cell anaemia in vidarbha region

2019

International Journal of Pharmaceutical Research

Chandak, P and Vagga, A and Chaudhary, G A

Background: Sickle cell anaemia is an autosomal recessive disease wherein amino acid at the 6th position of the chain is replaced by some other amino acid. In this disease, the shape of erythrocytes is changed from oval to sickle cell. First time the sickle cell anaemia was considered as a haematological disorder more than 100 years ago and as a molecular disorder in 1949. Objectives 1) To know the status of blood gas profile in homozygous and heterozygous patients of sickle cell anaemia. 2) To know the count of RBCs, WBCs and platelets in homozygous and heterozygous patients of sickle cell anaemia. 3) To know the concentration of haemoglobin in patients of homozygous and heterozygous sickle cell anaemia. 4) To know the electrophoretic pattern in patients of homozygous and heterozygous sickle cell anaemia. Methodology: It will be a diagnostic type of study wherein 4 parameters will be assessed. they are blood gas levels, complete blood count, haemoglobin levels and electrophoretic patterns. Sample size of 60 patients will be taken which would then be divided into 2 groups. Their reports would be studied upon thereafter. During analysis tests like Chi square test and studentâ€™s unpair test will be performed along with excel sheets, bar graphs, etc. Results: The expected results are occurrence of low levels of Haemoglobin, Complete blood count and blood gas. Also, abnormal electrophoretic patterns are expected.

36. Profile of adolescents with severe anemia admitted in a Tertiary Care Hospital in Northern India

2011

Indian Journal of Pediatrics

Patra, S and Pemde, H K and Singh, V and Chandra, J and Dutta, A

Anemia is common during adolescence. However, severe anemia is uncommon and can have varied etiology. This study was conducted to find out the profile of adolescents (10-18 years) admitted for severe anemia. The Case records of children between 10 and 18 years old admitted during the year 2008 in Kalawati Saran Children's Hospital for severe anemia as admitting diagnosis were reviewed. There were 40 patients admitted with severe anemia during the year 2008. This constituted 3.37% of all the admissions. Mean age of these patients was 12 (+/-2.5) years and mean hemoglobin at admission was 3.6 (+/-1.4) g%. Megaloblastic anemia was most common type of anemia (42.5%) followed by aplastic anemia (27.5%) and 15% cases were due to severe iron deficiency anemia.

Although iron deficiency anemia is the most common type of anemia, but in adolescents megaloblastic anemia and aplastic anemia should be looked for whenever the adolescents present with severe anemia. Â© 2010 Dr. K C Chaudhuri Foundation.

37. Pattern and profile of pulmonary dysfunctions in patients of sickle cell anemia in central India

2015

Indian Journal of Physiology and Pharmacology

Tripathi, S and Khandelwal, E and Sinha, N and Khandwal, O

Background: Pulmonary dysfunctions due to sickle cell disease (SCD) are one of the leading cause of morbidity and mortality in central India. Although hypoxemia and respiratory disease are risk factors for vaso-occlusive crisis in patients with SCD, the mechanisms remain unclear. Obstructive and restrictive pulmonary changes develop in patients with SCD, but reports conflict as to the type of change that predominates. Objective: To compare pulmonary functions of SCD patients with controls and to understand the pathophysiology & pattern of distribution of pulmonary dysfunctions in SCD. Material and Methods: 140 patients of age 10 to 58 years and 151control of age 10 to 60 years were compared for pulmonary functions. Both groups were investigated for complete Hemogram, Echocardiography, Sickling test, Hemoglobin (Hb) electrophoresis. The results were statistically analyzed. Results: SCD group FVC, FEV1, PEF, FEF25%-75% and MVV were lower as compare to control groups in both sexes. The difference in FEV1, PEF, and FEF 25%-75% is statistically significant ($p < 0.05$) after the age of 20 years and in FVC after the age of 30 years in both the sexes. MVV was statistically significant after 20 years of age in females and 30 years in males. Obstructive, restrictive and mixed patterns of lung function abnormalities were observed, of which the restrictive pattern was predominant. Conclusion: Pulmonary function is abnormal in Patients with Hb-SS & AS. It is likely that abnormal pulmonary function reflects intrinsic lung disease in these patients and that the mechanisms are more complex in this population than originally appreciated.

38. Red blood cell alloimmunisation in transfuon dependent patients population-a study from eastern India

2014

Transfusion Medicine

Mukherjee, S and Sankha Datta, S and Bhattacharya, P

Out of 500 cases, 215 were male and 285 were female. 303 were from beta-thalassemia major, 150 were from E-beta thalassemia, 26 had aplastic anemia, 8 patients had sickle beta thalassemia, 12 had myelodysplasia and only 1 patient had sickle cell anemia. A total of 28 patients developed RBC allo immunisation (5.6%). Alloantibody against c had the highest incidence (28.57%) followed by E (21.42%), Jkb (7.14%), Jka (3.57%), C (3.57%), D (3.57%), and s (3.57%) respectively. 5 out of 28(17.85%) developed antibodies against c and E, and one against each of the following combinations; C and D (3.57%), E and Jkb (3.57%), E and Fyb (3.57%). The rate of alloimmunisation was highest in 31 to 40 years of age group (36.36%). No significant difference observed in rate of alloimmunisation among male & female patients' population ($P > 0.05$) and between beta thalassemia major and E-beta thalassemic patients (6.27% vs. 6%, $P > 0.05$). Conclusion: Overall incidence of RBC alloimmunization in the transfused dependent patients' population was 5.6%. Thus, pretransfusion antibody screening on patients' sample prior to crossmatching needs to be initiated in Eastern India to ensure safe transfusion practice.

39. Frequency of vasocclusive crises and the relationship of vitamin d deficiency to the frequency of pain crises in children with sickle cell disease in an aboriginal tribal region in Gadchiroli, India

2017

Blood

Jain, D and Jaiswal, S and Bakshi, N and Krishnamurti, L

Background Recent reports suggest that the clinical phenotype of sickle cell disease (SCD) in India may not be as mild compared to African haplotypes as previously believed (Jain et. al. 201 6). There is however a paucity of data from India.There are some reports of association between Vitamin D deficiency and pain in SCD, but these associations have not been studied in pediatric SCD patients form India. The objective of this community-based study was to determine the frequency of vaso-occlusive episodes (VOE) in Indian pediatric SCD patients and to determine the relationship of Vitamin D deficiency to the frequencies of VOE and other SCD complications. Methods We conducted a community based study in aboriginal tribal area in Gadchiroli district in Maharashtra State, India. After providing informed consent, patients completed a health history interview and underwent blood testing for serum 25-Hydroxy Vitamin D by Radioimmunoassay. The number of times in the previous year that their child had severe pain, associated with cessation of activity including play and school attendance which required treatment, in the past year, was obtained by parent self-report, and was defined as a VOC. Hospitalizations for VOE treatment and number of blood transfusions in the past year were also obtained by parent self-report. No medical record review was done. Descriptive statistics and tests of hypothesis were performed using STATA Ver. 13. Results We screened 91 children (50% male) with a median age of 14 years (range 5-1 6, IQR 1 0-1 6). They reported a median 3 episodes of VOC/Year (IQR 2-4) and a median 2 Hospitalizations (IQR 1-2) and a median of 1 blood transfusion/year (IQR 1-2). Median Vitamin D level was 26.4 (IQR 22.6-29.9) with 1 5 patients (1 6.5%) being Vitamin D deficient (<20ng/ml). On Student T-test with equal variance, Vitamin D deficient patients vs. Vitamin D replete patients revealed 4Â±0 vs. 2.5Â± 0.97 VOCs/year (p=0.0000), 2.3Â± 0.7 vs.1.60Â±0.7 (p=0.0006). Hospitalizations for VOC/year(P=0.010) and 1.9Â±0.7 vs 1.4 Â±0.6 blood transfusions/year(P=0.0064). In a linear regression model, after adjusting for age and sex, higher vitamin D levels were associated with lower VOCs (P=0.0000, Model F statistic= 53.8). Conclusions: Children with SCD in an aboriginal tribal region in Gadchiroli, India have reported pain frequencies similar to that described in reports from other parts of the world. This suggests that the phenotype of SCD in India may not be as mild as previously thought. In this population, Vitamin D deficiency is associated with significantly increased VOE, hospitalizations for VOE and blood transfusions. These data provide the rationale for larger studies to further elucidate the association of Vitamin D with pain events in SCD, and to determine the causes of Vitamin D deficiency and its impact on severity of SCD, so as to inform the development of suitable preventive and therapeutic strategies.

40. Sickle cell disease in central India: High prevalence of sickle/beta thalassemia and severe dsiease phenotype

2015

Blood

Jain, D and Warthe, V and Colah, R and Serjeant, G R

Objectives: To assess the clinical, haematological and molecular features of sickle cell disease in central India where the disease has been reported to be more severe than the mild clinical course usually observed in the Asian haplotype of homozygous sickle cell (SS) disease. Methods: A cross-sectional assessment of 91 consecutive patients with sickle cell disease attending clinics at the Akola Government Medical College, Akola, Maharastra State, India. Results: Of the 91 patients, who were predominantly of the scheduled caste community, 49 had SS disease, 6 had sickle cell-HbD Punjab, and 36 had sickle cell-beta thalassaemia. Of the patients with sickle cell-beta thalassaemia, the beta thalassemia mutation was IVS1-5 G>C mutation in 25 patients (69%) while the rest had one of seven other molecular mutations identified (Table1). Contrary to commonly held beliefs, alpha thalassaemia occurred in only 9/90 (10%) of subjects but fetal haemoglobin (HbF) levels were markedly elevated with mean and median levels of 24.4%. All except 3 SS disease patients had the Xmn1(+/+) polymorphism. These

patients exhibited many of the severe manifestations of sickle cell disease. Comparison of SS disease and sickle cell-beta thalassaemia showed no differences in the prevalence of dactylitis, bone pain crisis, acute chest syndrome, haemoglobin level, reticulocyte counts or hydroxyurea usage but patients with sickle cell-beta thalassaemia had significantly more hospital admissions, blood transfusions, and greater frequencies of splenomegaly and hepatomegaly. Conclusions: Many of the patients with sickle cell disease in central India appear to have relatively severe manifestations. This appears to be due to much lower frequencies of alpha thalassaemia and more frequent sickle cell-beta thalassaemia. There is a need for assessment of the indications and policies for blood transfusion and for hydroxyurea.

41. **Hemoglobinopathies in Dharwad, North Karnataka: A hospital-based study**

    2008

    Journal of Clinical and Diagnostic Research

    Shivashankara, A R and Jailkhani, R and Kini, A

The inherited disorders of hemoglobin are responsible for an extremely complex series of clinical phenotypes. Sickle cell anaemia and thalassemia can cause chronic ill-health and life-threatening situations. Present study was carried out at Dharwad of North Karnataka. The practice of consanguineous marriages is an accepted sociocultural phenomenon in this region. This study was hospital-based and the paediatric cases of hemoglobinopathies were identified based on clinical data, family history, red blood cell indices and hemoglobin electrophoresis. Out of the fifty cases twenty chidren were carriers of beta- thalassemia trait and fifteen children were suffering from beta-thalassemia major. Two cases of sickle cell trait and lone case of a compound heterozygote for HbS/beta-thalassemia were also identified. Families of four cases of hemoglobinopathies were studied in detail to identify the carriers of abnormal hemoglobins. Ten out of fifty children of the study were products of consanguineous mating. The population of Dharwad appears to be a repository of thalassemia. An extensive screening of the population is needed to assess the prevalence of hemoglobinopathies, which will help in identification of carriers of hemoglobinopathies and further in taking adequate therapeutic and preventive measures.

42. **Genetic structure of human populations based on 5 gene loci: A preliminary report from Northern India**

    2016

    Gene Reports

    Fareed, M and Afzal, M

The genetics of human populations reveals the evolutionary causes of population structure, population history, human diversity, racial divergence, adaptation, cultural and social behaviors and understanding human adaptation to local environmental constraints. The study aimed to determine the genetic relationship among six human population of Jammu and Kashmir, Northern India. This preliminary effort involved five gene loci of genetic traits, viz. ABO and Rh blood type, phenylthiocarbamide, color blindness and sickle cell trait. A total of 3679 healthy subjects were selected from six Muslim populations viz., Gujjar and Bakarwal (nÂ =Â 762), Mughal (nÂ =Â 560), Khan (nÂ =Â 642), Malik (nÂ =Â 564), Mir (579) and Syed (nÂ =Â 572). The allele frequencies and heterozygosity levels show significant differences among six populations (pÂ <Â 0.05). The phylogentic tree revealed that Mughal and Gujjar and Bakarwal (tribal population) are close to each other and differ from other four populations (Malik, Mir, Khan and Syed). Further studies in context genomic diversity, history and origin of these populations will be undertaken in future to get more conclusive proof.

43. Renal involvement in sickle cell disease in tribal Western India

2015

Nephrology Dialysis Transplantation

Patel, M and Kute, V and Ugale, P and Valvi, R

Introduction and Aims: Sickle cell disease (SCD) is the most common hemoglobinopathy. Renal abnormalities in SCD are well known and include urinary concentration defect, acidification defect, renal papillary necrosis and proteinuria related to glomerular injury leading to chronic kidney disease. North Maharashtra in India is considered as a sickle belt and strict practice of endogamy in all social ranks may be a reason for its common occurrence in this region. The study is undertaken to assess the renal involvement in sickle cell disease patients. Methods: This is a prospective observational study involving 65 patients of SCD from November 2013 to July 2014. All patients underwent evaluation of renal function and urine examination to detect proteinuria and other urinary abnormalities. Estimation of glomerular filtration rate (GFR) was done by the criteria of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Results: The patient population consisted of 30 males (46.2%) and 35 females (53.8%). The median age was 21 years (Range: 10-37 years). Glomerular hyperfiltration was present in 15 patients (23%), while low GFR (less than 60ml/min/1.73m2) was found in 9 patients (13.8%). Of the patients with low GFR, rise in creatinine was seen in only 4 patients. Microalbuminuria (30-300 mg/day) was seen in 20 patients (30.8%) and macroalbuminuria (more than 300 mg/day) in 5 patients (7.7%). Microscopic hematuria was detected in 16 patients (24.6%) and hemoglobinuria 6 patients (9.2%). Hyperkalemia was observed in 9 patients (13.8%) and all had urinary concentrating defect. The comparison between patients according to GFR and hematological parameters showed that patients with hyperfiltration were younger, high hemoglobin and lower creatinine levels while patients with low GFR were elder, anemic and renal dysfunction. Conclusions: Renal involvement in SCD is common with proteinuria (microscopic and macroscopic) being the commonest abnormality. Though GFR decreases, serum creatinine may remain low suggesting to take precautions while using analgesics. Considering these abnormalities, routine screening of SCD patients is indicated to prevent further progression of renal disease.

44. Sonological evaluation of abdominal organs in sickle cell crisis in Western Orissa

2004

Indian Journal of Radiology and Imaging

Mohanty, J and Narayan, J V S and Bhagat, S and Panda, B B and Satpathi, G and Saha, N

Objective: Sickle cell disease (SCD), being prevalent in the western belt of Orissa, the following study was undertaken to evaluate the various spectrum of abdominal sonographic findings involving the liver, spleen, gall bladder and kidneys. Materials and methods: The study included fifty patients of SCD presented with acute symptoms of sickle cell crisis. Results: The most frequent US findings in the study were: hepatomegaly (72%), splenomegaly (64%) and cholelithiasis (22%). 22% of patients presented with splenic infarction, 10% patients showed splenic calcification. Increased bilateral renal echogenicity was observed in 16% of patients. Conclusions: To conclude ultrasonography is a readily accessible and non invasive method for the evaluation of different abdominal organs.

45. Thalassemia: Bridging the gap between prevention research and practice

2016

International Journal of Laboratory Hematology

Agarwal, S and Arya, V and Kumar, R and Gupta, U and Tripathi, P and Gautam, S

Introduction: Introduction: b-thalassemia, is caused by the decreased production of normal b-globin chains and is extremely common in Mediterranean, middle eastern, South East-Asian & black Africans countries. More than

200 point mutations and rare deletions in the b-globin gene accounting for these b-chain deficiencies have been characterized, and result in reduced levels (b+-thalassemia) or complete lack (b0-thalassemia) of the encoded b-chains. It is a major public health problem in India where the Î²-thalassemia carrier frequency is 3-17% in different regions and 15,000 affected children born every year. Methods: Methods: All referred anemia cases from Genetics OPD, SGPGI, Lucknow, India from 1995- 2015 were evaluated for red cell indices, G6PD, Pyruvate Kinase and iron deficiency. Further to characterize the mutations present in the patients defined clinically and at hematological level as beta thalassemia, DNA was isolated from the peripheral blood. bglobin gene was amplified by using ARMS-PCR technique followed by visualization of the bands on agarose gel electrophoresis. Later the mutations were confirmed on Sequencing. These samples have already been checked for hemoglobin variants by Bio-Rad CE-HPLC dedicated to hemoglobin variant analysis. Results: Results: We have done the molecular characterization of the 10,000 chromosomes, out of them 75.0% chromosomes accounts for common mutations, 9.0% for less common mutations while rare and new mutations are covered by 1.3% chromocomes.12.4% chromosomes are affected by other hemoglobin variants (Hb S,Hb E & Hb D). 2.3% chromosomes still remain uncharacterized. The prenatal diagnoses for beta thalassemia since the introduction of service at our centre were studied. Chorionic villus sampling was performed at 10- 12 weeks gestation. PND was done by ARMS PCR or direct sequencing when required. DNA analysis of the 320 cases where prenatal diagnosis was provided, revealed 80(25.0%) affected fetus, 164 (51.25%) carriers & 76 (23.75%) fetuses as normal. Couples having affected fetus were counseled suggestive to terminate the pregnancy. Conclusions: Conclusion: These results indicate that analysis of the DNA samples for the beta globin gene mutations could provide good coverage for bthalassemia carrier screening & prenatal diagnosis. These are the two best options along with awareness program to run at state level to prevent the birth of homozygous beta thalassemia in the country.

46. Pos-306 prevalence of renal dysfunction in primitive tribal groups in utnoor (telangana)

2021

Kidney International Reports

Bukka, V and Taduri, G and Kaldindi, R K and Guditi, S and Das, U and Chinnaparthi, P R and Thoom, P R and Thorrem, R and Herur, S and Kinjarapu Naidu, S

Introduction: India has the largest concentration of tribal populations globally. According to the Census of India 2011, the tribal population of India is 8.6 per cent of the total population which is about 67.8 million people Particularly vulnerable tribal group (PVTG) (earlier: Primitive tribal group) is a government of India classification created with the purpose of enabling improvement in the conditions of certain communities with particularly low development indices. During the fourth Five Year Plan a sub-category was created within Scheduled Tribes to identify groups that considered to be at a lower level of development This sub-category was named "Primitive tribal group"(PTG). The features of such a group include a pre-agricultural system of existence, that is practice of hunting and gathering, zero or negative population growth, extremely low level of literacy in comparison with other tribal groups. Groups that satisfied any one of the criterion were considered as PTG and by the conclusion of the eighth five-year plan, a total of 75 tribal groups were identified as PTG. The Global Burden of Disease, Injuries and Risk Factors (GBD) study has provided a state-of-the-art understanding of the global burden for many conditions, including chronic kidney disease (CKD). CKD has resulted in almost one million deaths worldwide, and is the direct cause of one out of 57 fatal outcomes. It remains among the few growing causes of mortality which made CKD the 13th leading cause of death in 2013; this compared to ranking 27th in 1990, signifying a rise of 134% over this period. There is a dearth for prevalence studies on CKD in India. This necessitates population targeted research in this avenue. The aim of the present study was to estimate the prevalence of renal dysfunction in primitive tribal groups, residing in areas that come under ITDA Utnoor, Telangana. Our other Objective was to study the data generated for possible etiologies of CKD in the given population. Methods: Inclusion Criteria: The primitive tribes residing in areas that come under ITDA Utnoor in Telangana. Exclusion Criteria: Non tribal population residing in the area. Methodology: â€¢ Basic demographic data and clinical examination â€¢ Following Blood tests were performed: â€“ CBC â€“ Creatinine â€“ Lipid profile â€“ LFT â€“ Blood sugars Nestrof and Solubility. Results: Total population of PVTGâ€™s screened: 14041 Volunteers with renal dysfunction: 1108 Number of subjects with Renal Dysfunction with age <10years: 562 Number of subjects

with Renal Dysfunction between 11-18 years: 89 Number of subjects with Renal Dysfunction with age >18 years: 457 Mean age:24.4 years Mean GFR: 42.4 ml/min Etiologies of renal dysfunction in PVTGâ€™s: CKD-U (60%), HTN-nephrosclerosis (33%), Sickle cell nephropathy (5%), Diabetic nephropathy(1.1%) Prevalence of co-morbitities among subjects with renal dysfunction: Diabetes: 12 (1.1%) HTN: 178 (33%) Anemia: 778 (70.2%) Sickle cell anemia: 41 (5.3%) Low BMI: 216 (47.3%) [Formula presented] Conclusions: Prevalence of renal dysfunction among PVTGâ€™s is 7.9%, with maximum prevalence among subjects with 6-10 years of age, CKD-U being the most common cause of renal dysfunction followed by Hypertensive nephrosclerosis and Sickle cell anemia, while the prevalence of diabetic nephropathy being low. No conflict of interest

47. Prevalence of inborn errors of metabolism in neonates

2018

Journal of Clinical and Diagnostic Research

Sharma, P and Kumar, P and Tyagi, M S and Sharma, R and Dhot, P S

Introduction: Among the most advanced public health promotion and disease prevention programs, the newborn screening is of paramount importance, seeking timely detection, diagnosis and treatment of genetic disorders which may otherwise lead to serious consequences upon the health of newborn. Aim: To evaluate the prevalence of Inborn Error of Metabolism (IEM) disorders among neonates of various ethnic or racial groups from east, west, north and south, zones of India through newborn screening. Materials and Methods: A cross-sectional, population based prospective study was conducted at PreventiNe Life Care Laboratories, Navi Mumbai, Maharashtra, India. Study was conducted for a period of three years from October 2012 to November 2015. Mass screening of newborn blood samples was done via TMS/GCMS/Enzyme assay/HPLC/ELISA technique. The blood and urine samples were used for analysis. The samples have been collected from 150 locations through various hospitals across India. Samples obtained were categorised zone wise (east, west, north, south zones of India). For analysis of blood, samples were collected by heel prick method. Results: In the present study, 2.9% prevalence (of the total 70,590 samples analysed, 2053 cases were found positive) of IEM was observed. Of these positive cases, 13% (279 of 2053 positive cases) cases belonged to eastern zone, 24% (493 of 2053 positive cases) were from northern zone, 38% (793 of 2053 positive cases) were from southern zone and 23% (488 of 2053 positive cases) were from western zone. Among these, the highest prevalent disorder was found to be G6PD deficiency, with 1.3% (923 positive of 70,590) cases reported followed by haemoglobinopathies, 0.5% (360 positive of 70,590) and congenital hyperplasia with 0.34% (239 positive of 70,590) cases of the total newborns, screened. Conclusion: The newborn screening is expanding its wings throughout the world. The outcome of present data offers a unique opportunity to explore the birth prevalence of inborn metabolic disorders in the current population. Understanding the birth prevalence of these disorders in India from its various zones will definitely improve the short term and long term medical needs faced by affected communities.

48. Association of sickle cell anaemia in morphology of full term placenta in Chhattisgarh region

2012

Biomedical Research

Praveen, K and Amit, K and Yogesh, A S and Shukla, C K and Banergee, C and Singh, T

Placental examination reflects prenatal factors and postnatal fetal outcomes. In the present study 100 full term placentas were studied morphologically in which 50 placentae were collected from normal mothers and 50 were from mothers with sickle cell disease. Placentas were examined for shape, weight and volume of placenta with surface area number of cotyledons, attachment of umbilical cord. No change was observed in cotyledon count in placentas of sickling cases. The most common shape of the placenta was discoidal in both normal cases (68%) and in mothers with sickle cell disease (50%). The second most common shape of the placenta was oval and it was found significantly higher in mothers with sickle cell disease (32%) than in normal cases (22%). Irregular shape was found in only 6% of normal placenta while it was 16% in cases of sickling cases which was significantly higher. Most commonly attachment of umbilical cord was central (32%) in normal cases and near centre in

sickling cases (36%). The weight of placenta was significantly lower in cases of sickling (mean 438.08gm) in comparison to normal subjects (mean 468.88gm). The mean volume of placenta was also significantly lower in case of sickling cases (mean 502.06 ml) in comparison to normal subjects (mean 576.44ml). The placental surface area was also affected by sickle cell anaemia and it was found lower (mean 262.14cm2) than normal subjects (mean 273.12cm2). Thus, the present study indicated that sickling adversely affected gross placental parameters. This might be the probable reason behind worst foetal outcome in mothers with sickle cell disease.

49. Thalassemia carrier detection during antenatal period : Single centre experience from Eastern India

2018

Indian Journal of Hematology and Blood Transfusion

Ghosh, M and Basu, K and Sengupta, M and Mukhopadhyay, M and Chatterjee, U and Datta, C and Biswas, A

Aims & Objectives: Haemoglobinopathies include thalassemias and structural variants of hemoglobin affecting nearly 3 to 4 lacs of newborns per year. The present study was conducted in a tertiary care centre of eastern India to evaluate the epidemiology and earlier detection of carrier stages of haemoglobinopathies among antenatal mothers undergoing routine screening. Patients/Materials & Methods: This single centered, prospective, cross sectional study was conducted amongst the antenatal mothers visiting the Thalassemia Control Unit for a duration of 3 years, on a total of 7340 study population. The database was collected using a Linux Based Thalamon Software. Results: Out of a total number of 7340 subjects, on HPLC study, 91.7 % were diagnosed as normal, 0.039% were diagnosed as Î² thalassemia carriers,0.038% as HbE carrier and 0.0038% were diagnosed among others as HbD carriers, HbS carrier and HPFH traits. HbA2 levels were found to be higher among the carrier stages in comparision to the normal individuals. Among the different haematological parameters assessed MCV showed maximum variation The hematological parameters of Hb D carrier showed greatest variations with respect to the lower and upper confidence intervals. Î² thalassemia carrier showed the most significant decrease in the mean levels of all the parameters as compared to the normal individuals. Discussion & Conclusion: To reduce the global disease burden, identification of the carriers becomes essential, especially in the antenatal mothers. Cation exchange HPLC (CE-HPLC) serves as an appropriate tool for identification and quantification of normal Hb and its abnormal variants at its earliest. An effort is to create a mass awareness for detection of carrier states among antenatal mothers and further follow up is indispensable to reduce the immense disease burden of hemoglobinopathies.

50. Profile of childhood chronic pancreatitis in coastal eastern India

2011

Pancreatology

Das, H S and Misra, B and Panigrahi, M K and Kar, S K and Panda, C and Singh, S P

Background: Childhood chronic pancreatitis is not common in coastal eastern India. Aim: To undertake a retrospective study of the clinical profile, etiology and response to treatment of the cases of chronic pancreatitis in paediatric population. Methods: The retrospective study is an analysis of consecutive patients with chronic pancreatitis (CP) under the age of 15 years who attended the Department of Gastroenterology over a period of 2 years. Results: Total no of cases studied were 10 in number of those 60% were males while 40% were females with sex ratio (M:F) of 3:2. The age at presentation ranged between 8-14 years with a mean age of 11 years. The most common presentation was pain abdomen seen in 80% cases, followed by steatorrhoea in 30%, and ascites in 40% cases. Sixty percent of children had multiple calculi. One patient had pleural effusion with pancreatic ascites. A patient of sickle cell disease with uncontrollable pain and ascites improved following surgery and another case of autoimmune pancreatitis is on steroid. One patient was diabetic at presentation and now on insulin. Conclusion: Childhood pancreatitis accounted for 6% cases of all cases of chronic pancreatitis in our study. Most of them were calcific in nature. Pancreatic ascites was more prevalent in childhood pancreatitis as compared to adults.

51. Prevalence of beta thalassemia among various tribal population of West Bengal

2011

Indian Journal of Hematology and Blood Transfusion

Chakraborty, A and Bhattacharyya, D and Basak, J and Mukhopadhyay, S and Mukhopadhyay, A

Introduction: Thalassemia has emerged as one of the most common health problems among the tribal populations in West Bengal. This study is aimed to observe the spectrum of various beta mutations among tribes prevalent in different districts of West Bengal. We mainly confronted with the Sardar tribes in extreme south of West Bengal. There were Toto, Rabha, Oraon, Munda and Nagbanshi in North Bengal who underwent the screening of Thalassemia carrier status. Materials & Methods: From January 2009 to June 2011, 1,217 tribes were screened. Mass awareness programmes were followed by collection of peripheral blood samples in EDTA vials and transported to the laboratory in ice packs. NESTROFT, CBC and HPLC were done for all samples. ARMS PCR was performed to detect point mutations in case of beta mutations. Results: Among 1,217 tribes screened, 305 were HbE carrier, 121 HbE homozygous, 96 beta carrier, 19 beta patients & 12 were sickle cell anemia. Rests of the individuals screened were normal and many of them were suffering from iron deficiency anemia. Conclusions: Molecular Characterization of Beta globin gene mutations among these tribes have confirmed the presence of the following mutations: IVS-1 nt5 (G>C), IVS-1 nt1 (G>T), codon 15 (G>A), codon 26 (G>A), the mutation which leads to HbE. The most common mutation observed among Totos and Rabhas were codon 26 (G>A) of North Bengal. The mutation IVS-1 nt5 (G>C) is prevalent among the Oraon, Nagbanshi and Sardar tribes of Bengal. The other mutations which are present among them are codon 15 (G>A) and codon 30 (G>C). Our results have added to the existing data on the common beta globin gene defects which are prevalent among the general population of West Bengal, India.

52. Multiorgan dysfunction syndrome in sickle cell disease.

2005

The Journal of the Association of Physicians of India

Hiran, S

OBJECTIVE: Concurrent failure of multiple organs in patients of sickle cell disease (SCD) has rarely been reported. The main objective of this study was to highlight the multiorgan dysfunction (MODS) that occurs in some patients during sickle cell crisis. METHODS: Ten episodes of multiorgan failure were identified with sickle cell disease and defining criteria of organ failure of two or more organs that is lung, liver, or renal were established according to Acute Physiological and Chronic Health Evaluation - II (APACHE-II) criteria. RESULTS: Most episodes occurred during vaso-occlusive crisis, which was associated with a severe pain event. The onset of organ failure was associated with fever, rapid fall in haematocrit, platelet count and altered sensorium, later organ failure set in. Respiratory, hepatic, and kidney failure (all the three organs) were present in three of the ten patients who were in sickle crisis. Of this we lost one patient despite exchange transfusion and ventilator support. Of the four patients who had respiratory failure accompanied by hepatic failure, one patient died due to associated septicemia. Respiratory failure with renal involvement was seen in two patients whereas hepatic and renal failure was present in only one patient. Except for two, all other patients improved after aggressive blood transfusions. CONCLUSION: Acute multiorgan failure is a life threatening complication of SCD, which can exhibit without any evidence of chronic organ damage and is easily reversed by prompt and aggressive transfusion therapy.

53. Study of peripheral neuropathy in patients with sickle cell disease

2013

Indian Journal of Physiology and Pharmacology

Dash, S

Objective: To find out the correlation of peripheral nerve involvement in patients with sickle cell disease through nerve conduction study. Method: Thirty patients (M=23, F=7) with established sickle cell disease were taken in the present study for nerve conduction study. All were within the age group 15-45yrs.They were closely scrutinized for sign and symptom of clinical neuropathy. It was found that only 10 cases had features of clinical neuropathy. The control group contains 30 normal person within the same age group(M=20, F=10).A comparative study of nerve conduction velocity were done between sickle cell disease patients with neuropathy and without neuropathy and also compared with normal laboratory value. The study include the following things: a) motor nerve conduction study; b) sensory nerve conduction study;c) F wave; d) terminal latency Results: In the present study motor nerve conduction velocity (MNCV meter/sec) and sensory nerve conduction velocity (SNCV meter/sec) in different nerves were compared with laboratory value (30 normal persons). The mean MNCV was delayed in patients with neuropathy when compared with sickle cell disease without neuropathy and also with normal laboratory value ($p<0.001$).Similarly mean SNCV was delayed in patients with neuropathy when compared with sickle cell disease without neuropathy and also with normal laboratory value ($p<0.001$). It was observed that terminal latency of MNCV is prolonged ($p<0.05$) in sickling patient with neuropathy. In patients with clinically evident root involvement did show prolongation of F wave as compared without root involvement. Conclusion: The sickle cell disease, an inherited disorder is said to be having world wide distribution but its prevalence is restricted to some areas of few developing countries. In India sickle cell disease is common in Western Odisha. Recurrent vasoocclusive crisis is well established complication of sickle cell disease. The nerve roots and peripheral nerves may like wise be damaged due to vasoocclusive crisis. Nerve conduction study is useful for early detection of neuropathy and also be used to test the progression and effect of treatment in patients having sickle cell disease with neuropathy.

54. Thrombophilic profile in extrahepatic portal vein obstruction-experience from a tertiary centre in India

2015

Journal of Thrombosis and Haemostasis

Dhiman, P and Saxena, P and Bihari, C and Rastogi, A and Sarin, S K

Background: In India, extrahepatic portal vein obstruction (EHPVO) is responsible for about one third cases of adults and more than half of the cases in children as a cause of portal hypertension. Role of various thrombophilic markers and treatment strategies are not clearly established. Aims: To study the thrombophilic profile, treatment and outcome of patients with EHPVO. Methods: A retrospective study of patients with EHPVO who visited the tertiary care centre was conducted. Characteristics of clinical presentation, etiology of EHPVO, management and outcome were analyzed. Results: A total of sixty seven cases were diagnosed with EHPVO during last 2 years. Out of these, 45 were males and 22 were females. Mean age of presentation was 31.9 Â± 13.9 years. Clinically, most of the patients 32 (48%) presented with pain abdomen followed by upper GI bleeding in 18 (26.8%) cases. Thrombophilia work up done showed risk factors in 44 (65.7%) cases which include Protein S deficiency in 24 cases mean value (36.3 Â± 13.07), Protein C deficiency in 2 cases, homozygous methyltetrahydrofolate reductase in 3 cases, homozygous JAK2V617F mutation in one case and hyperhomocysteinemia in 16 patients (8 cases had associated Protein S deficiency). Work up for antiphospholipid syndrome was done in 46 cases out of which three patients showed significant antiphospholipid and anticardiolipin Ig M levels. One patient was diagnosed as immune thrombocytopenia and one patient was a diagnosed case of sickle cell trait. None of the patients was positive for Prothrombin G20210A mutation and one patient was heterozygous for Factor V Leiden. Treatment: Shunt operations done in five patients because of uncontrolled bleeding. Anticoagulation was started in cases of acute thrombosis and duration was decided with regard to risk to benefit ratio in each case. Conclusion: This study concludes that concurrence of prothrombotic disorders is more common than expected and studies are needed to guide the duration of anticoagulation.

55. Spectrum of thalassaemia syndromes and structural hemoglobin variants encountered in a referral hospital in North India

2010

British Journal of Haematology

Das, R and Kaur, J and Marwaha, I and Ahluwalia, J and Trehan, A and Malhotra, P and Marwaha, R K and Varma, S and Garewal, G

The major globin genes (alpha, beta, gamma and delta) undergo mutations to produce thalassemia syndromes or hemoglobinopathies. We analyzed the various thalassemias and hemoglobinopathies encountered in our department in sixteen years from 1993-2008. A total of14,000 samples were screened and 1201 cases ofthalassemia major (8.6%), 3973 beta thalassemia trait (bTT, 28.5%) were encountered. Thalassemia intermedia syndrome with combinations of a and b gene defect constituted 286 patients (2%) who required variable numbers of blood transfusions. Of the sickle cell syndromes, 22 patients were homozygous, 40 were double heterozygous with b thalassemia and 76 cases had sickle cell trait. Seventy nine patients with double heterozygosity for Hb E and b thalassemia were variably symptomatic and heterozygous Hb E was noted in 73 individuals. Majority of the patients of sickle cell syndrome or Hb E syndromes were referred cases from Bihar, Bengal, Orissa, Assam or North East. Hb D Punjab was noted in heterozygous state in 116 and double heterozygosity with bTT was in 63 individuals. An interesting combination of nine patients with double heterozygosity for Hb S and Hb D Punjab was noted and all these patients behaved clinically as moderate thalassemia intermedia. Other unusual cases encountered were Hb Q India, Hb J Meerut, Hb D Iran, Hereditary persistence of fetal hemoglobin and delta beta thalassemia. One single case of Hb Evanston, Hb Chandigarh and Hb Sabine which were detected by DNA sequencing was seen. Many of these variants are either Î± or Î² chain defects at different locations which result in change in amino acid and depending on the structural location of the protein the individual may remain asymptomatic or become symptomatic. The epidemiological spectrum of thalassemias and hemoglobinopathies are heterogeneous in Indians and is useful to study the pattern of population migration and admixture.

56. Prevalence of anemia on a backdrop of malaria ''A community based recent study''

2011

Indian Journal of Hematology and Blood Transfusion

Pati, S S and Rath, P K and Mishra, S K

Objective Sundargarh district of Odisha is known to be a highly endemic district for malaria mostly Plasmodium falciparum. Sickle cell gene is known to co-exist in the malaria endemic area. There is interplay of nutritional anemia, malaria induced anemia and coexistence of sickle cell disease in the area. The present study was designed to study the existence of anemia with a special reference to sickle cell gene prevalence. Materials &Methods: The study was conducted as a part of Corporate responsibility project of SAIL named "Chetna" From 1st March 2011. Village wise camps were organized to screen blood hemoglobin level by Hemocue, Solubility test to screen sickle cell in all age group. The positive cases for solubility were further evaluated by HPLC (D 10, Bio-Rad) to look for presence of hemoglobinopathy. Positive cases were provided counseling with their consent. Results: Total 5,300 persons were screened in different camp till 31-7-2011. The overall presence of anemia in Sundargarh district was found to be 78%. Severe anemia was 1.08%, moderate anemia 1.5% and mild anemia was the major contributor with 97.4% prevalence. Sickle cell trait was detected in 6% where as 1% of population had sickle cell disease. Conclusions: Anemia is mostly nutritional in the village population with extreme of age suffering the maximum. Sickle cell was less in Sundargarh district as compared to Sambalpur and Balangir district with high prevalence rate of 10-22%.

57. Morbidity Profile of Sickle Cell Disease in Central India

2013

Thalassemia Reports

Yadav, R and Singh, M P S S and Vishwakarma, C P and Neelkar, R L and Gupta, R B and Rajasubramaniam, S

Introduction: Sickle haemoglobin (HbS) in Madhya Pradesh is mainly confined to the tribal predominant areas. Out of fifty, thirty (32) two districts of MP (comprising of 240 blocks/ taluk) have sickle hemoglobin. The frequency of sickle cell trait varies from 3 to 35%. Materials and Methods: Till date no facilities for diagnosis exist at the district or PHCs. The patients remain undiagnosed. The Regional Medical Research Center for Tribals established the first clinic to identify and provide necessary aid to sickle cell disease patients at the NSCB Medical College, Jabalpur. The sickle clinic will identify the clinical profile and natural history of sickle cell disease in Central India and develop a simple protocol for its management and prevention. Results: A total of 691 sickle cell disease patients were registered in sickle cell clinic between 2002 and 2012. Majority of the registered patients were males (68.7%). About 46.7 % belonged to Scheduled caste category, Backward Class (29.1%) and Scheduled tribe (14.2%). About 73.1% of patients were demonstrated Splenomegaly. Splenectomy was observed in about 1.2 % of the patients. The most frequent clinical symptoms observed these patients was pallor (95.1%), Icterus (85.1%), joint pains (80.8%), fever (76.0%), bony pains (61.2%), abdominal pain (38.8%), joint swelling and chest pain (21.0%). General weakness was observed among (81%) patients. Nearly 50% of the patients reported at least one blood transfusion during their follow-up period. History of multiple blood transfusions was observed in about 16.5% cases. Majority of the patients (69.0%) reported onset of the disease prior to attaining the age of 6 yrs. Seventeen % patients showed first manifestation of the disease on or after 9 years of age. Conclusions: A reduction in severity of the disease was observed in the majority of cases post intervention. Percentage of severe cases were reduced and shifted to mild category consequent to intervention.

58. Prevalence of Î²-thalassemia and other haemoglobinopathies in six cities in India: A multicentre study

2013

Journal of Community Genetics

Mohanty, D and Colah, R B and Gorakshakar, A C and Patel, R Z and Master, D C and Mahanta, J and Sharma, S K and Chaudhari, U and Ghosh, M and Das, S and Britt, R P and Singh, S and Ross, C and Jagannathan, L and Kaul, R and Shukla, D K and Muthuswamy, V

The population of India is extremely diverse comprising of more than 3,000 ethnic groups who still follow endogamy. Haemoglobinopathies are the commonest hereditary disorders in India and pose a major health problem. The data on the prevalence of Î²-thalassemias and other haemoglobinopathies in different caste/ethnic groups of India is scarce. Therefore the present multicentre study was undertaken in six cities of six states of India (Maharashtra, Gujarat, West Bengal, Assam, Karnataka and Punjab) to determine the prevalence of haemoglobinopathies in different caste/ethnic groups using uniform methodology. Fifty-six thousand seven hundred eighty individuals (college students and pregnant women) from different caste/ethnic groups were screened. RBC indices were measured on an automated haematology counter while the percentage of HbA2, HbF and other abnormal Hb variants were estimated by HPLC on the Variant Hemoglobin Testing System. The overall prevalence of Î²-thalassemia trait was 2.78 % and varied from 1.48 to 3.64 % in different states, while the prevalence of Î²-thalassemia trait in 59 ethnic groups varied from 0 to 9.3 %. HbE trait was mainly seen in Dibrugarh in Assam (23.9 %) and Kolkata in West Bengal (3.92 %). In six ethnic groups from Assam, the prevalence of HbE trait varied from 41.1 to 66.7 %. Few subjects with Î´Î²-thalassemia, HPFH, HbS trait, HbD trait, HbE homozygous and HbE Î²-thalassemia as well as HbS homozygous and HbS-Î²-thalassemia (<1 %) were also identified. This is the first large multicentre study covering cities from different regions of the country for screening for Î²-thalassemia carriers and other haemoglobinopathies where uniform protocols and methodology was followed and quality control ensured by the co-ordinating centre. This study also shows that establishment of

centres for screening for Î²-thalassemia and other haemoglobinopathies is possible in medical colleges. Creating awareness, screening and counselling can be done at these centres. This experience will help to formulate a national thalassemia control programme in India. Â© 2012 Springer-Verlag.

59. Profile of liver fucntion test in sickle cell patients

2012

Indian Journal of Hematology and Blood Transfusion

Rath, M M and Panigrahi, M K and Sethy, S and Nayak, R and Mohanty, P and Gouda, K P and Pujari, S and Mohapatra, S R and Jena, R K

Introduction: Abnormal liver function tests are common in patients with sickle cell anaemia, even in the absence of liver disease.It may be hemolytic, cholestatic, hepatocellular and mixed pattern. There is a paucity of data on liver function in sickle cell disease (SCD) from this region. Aims and Objective: The present study aims at determinig the prevalance and the profile of abnormal liver fuction test in sickle cell patients. Material and Mathods: One hundred consucutive patients of sickle cell disease (homozygous)attainding the out patients department of hematology, S.C.B. Medical College from January 2012 to July 2012 were included in this study. Detailed clinical history was taken and subjected for complete blood count, hemoglobin profile, liver function tests, viral markers, ultrasonography of abdomen and pelvis. Results: The 100 patients included in the study ranged in age from 8 to 62 years (mean 30.8 Â± 9.11 years) and included 64 males and 36 females. Mean episode of vaso-oclusive crisis was 2.65 Â± 1.82 times and mean units of blood transfusion was 3.74 Â± 1.75. Mean hemoglobin concentration was 8.2 Â± 2.3 g/dl. Abnormality in liverfuction test was found in 86 % of the study participants. The mean serum total bilirubin, AST, ALT, ALP were 8.4 Â± 6.5 mg/dl, 104 Â± 43 U/L, 68 Â± 27 U/L, 258 Â± 76 U/L respectively. 49 %had hemolytic, 12 %had obstructive 25 %had mixed pattern of LFTs. On ultrasonography 24 % had hepatomegaly, 46 % had spleenomegaly, 11 % cholelithiasis and 2 % had both cholelithiasis and choledocholithiasis. Conclusion: Majority of sickle cell homozygous patients had abnormal liver fuction. One fourth of the patients had mixed pattern of LFTs that can not be explained by either hemolytic or obstructive component.

60. Haemoglobin-S in scheduled castes and scheduled tribes of Raipur (Madhya Pradesh) - a preliminary report

1980

Indian Journal of Medical Research

Tiwary, V K and Pradhan, P K and Agarwal, S

A total of 500 subjects belonging to scheduled castes and scheduled tribes of Raipur in Madhya Pradesh were screened for haemoglobin-S. The series included 170 hospitalised patients and 330 healthy subjects from the town. The overall frequency of positive sicklers was 18.6%; 17.6% of hospital patients and 19.4% of healthy subjects were found to be sickling positive. The frequency of positive sicklers among 310 scheduled castes was 17.7% and that among 190 scheduled tribes was 20.0%. Significant numbers of Mehtar (21 out of 90) and Bhangi (16 out of 70), among the scheduled castes, and Panka (9 out of 26) and Gond (19 out of 63), among the scheduled tribes, showed sickle cell haemoglobin. This preliminary study has revealed the existence of sickle cell gene among scheduled castes and scheduled tribes of this region.

61. Acceptance of prenatal diagnosis of sickle cell disease in a tribal population of Gujarat, India: A preliminary study at Valsad Raktdan Kendra

2011

American Journal of Hematology

Italia, Y M and Colah, R B and Ghose, K K and Diwanji, A and Mehta, V I and Raicha, B K and Mistry, A J and Desai, U D and Italia, K Y and Desai, D

Background: Haemoglobinopathies are a very heterogenous group of congenital hemolytic anemias. They include the Thalassaemias, structural variants such as haemoglobin S and hereditary persistence of fetal haemoglobin. Gujarat stands fifth in total tribal population (61.6 million) in India and according to initial survey of 10 million tribal population revealed 0.75% prevalence of Sickle Cell Disease amongst them. Based on this, it is estimated that 1500 new Sickle Cell Disease cases are added every year in Gujarat. Method: Solubility test and HPLC analysis were used for screening and couples at risk were counseled for prenatal diagnosis. Result: During last 36 months, 685 high risk antenatal women were screened and 428 (62.5%) were sickle heterozygous, 23 (3.3 %) were sickle homozygous and 7 (1 %) cases were Î² Thalassemia heterozygous amongst the tribal area of South Gujarat. An attempt was made for counseling these 458 positive cases and screening of their husbands. Out of them 364 (79.4 %) husbands have been screened with 75 (20.6 %) being sickle heterozygous and 9 (2.4 %) cases were Î² Thalassemia minor. Thus in spite of our best efforts during counseling only 84 high risk couples were found. Out of them only 31 (36.9 %) couples were eligible for prenatal diagnosis and 53 (63.1 %) were not eligible because they came after 20 weeks of pregnancy. Out of these 16 couples had prenatal diagnosis done at NIIH, Mumbai and 2 fetuses were affected with Sickle Cell Anemia and 1 with Thalassemia Major. 2 couples opted for termination of pregnancy while 3rd couple chooses to continue the pregnancy. Out of the 15 couples who were not ready for prenatal diagnosis, one couple had a precious pregnancy and had conceived after many years of marriage and the other 14 couples had problems such as family pressure, illiteracy, religious stigma, socioeconomically poor status. They came from very remote tribal areas and were not willing to travel up to Mumbai for prenatal diagnosis.

62. Pattern of sickle cell disorders: A study from a tertiary care centerin eastern part of India

2020

Blood

Sen, A and Dolai, T K and Gayen, T S and Roy, R and Sen, A and Mitra, S and Mandal, I and Roy, S and Bhattacharya, S and Neel Baul, S and Mandal, P K and De, R and Dutta, S

Introduction: Sickle cell disorders were originally found in the African regions, Arabian Peninsula and parts of India. However, in today's age of globalization patients with homozygous or compoundheterozygous Sickle cell disorders can be found all over the world. The objective of our study was toassess the distribution and clinical presentation of patients with Sickle homozygous or heterozygousdiseases in the Eastern part of India. Methods: Patients who attended the Thalassemia Clinic in our tertiary care center, between 1 st January 2018 to 31 st May 2020 (2 years and 4 months) were retrospectively analysed and the ones with a component of Sickle haemoglobin(HbS), either in the form of Sickle cell anemia/homozygousSickle cell disorders(SCA) or compound heterozygous diseases, like Sickle cell/Î² thalassemia(HbS/Î²), Sickle cell/Delta thalassemia(HbS/D), Sickle cell Haemoglobin/E thalassemia(HbS/E), wereincluded in the study. People having Sickle cell trait (HbS trait), have also been included. Thorough history of painful crises, blood transfusions, family history and treatment history waselicited and every patient was clinically examined. The patients were diagnosed by High PressureLiquid Chromatography (HPLC) or Thalassemia Mutation analysis by Polymerase Chain reaction(PCR). Results: A total of 95 patients with a component of HbS were considered as our study cohort, withHbS/Î² thalassemia patients being the majority (53.7%), followed by SCA (30.5%). Age of the studycohort ranged between 2-50 years age. HbS/Î² thalassemia patients presented at a later age (median17.5 years) than SCA patients (median 12 years). Their demographic distribution is depicted in Table 1. The most common clinical presentation was painful crisis (32,33.7%), be it abdominal pain (11,11.6%)or bone pain (13,13.7%). Other presenting complaints were pallor (26,27.4%), jaundice (12,12.6%) and fever (4,4.2%). Some rarer presenting manifestations were fatigue (4,4.2%), splenic infarction (1,1%),convulsions (1,1%), Raynaud's phenomenon (1,1%), headache (1,1%) or itchy skin lesions (1,1%). Fewpatients (4,4.2%) had recurrent pregnancy loss, and one patient was diagnosed incidentally duringan antenatal check-up. Most patients had more than one complaint. Very occasionally patientsrequired hospital admission, the reasons being, chest pain, fever, convulsions or abdominal pain. HbS trait was diagnosed incidentally during evaluation for other illnesses, most commonly duringevaluation of pallor (3,60%): one patient was later diagnosed with iron deficiency anemia. Most patients who attended our center were from within the state or neighbouring states. Thepatients were treated with Hydroxyurea, with/without blood transfusions,

chelation therapy withDeferasirox as required and Folic acid supplementation. People with HbS Trait continued to receiveFolate supplementation. Discussion and Conclusions: This study highlights the varied distribution of HbS among thepopulation attending a tertiary care center, irrespective of a specific area-based population. Till datemost studies conducted in India have highlighted the prevalence of Sickle cell disorders amongspecific focused populations. HbS/Î² thalassemia was the most common sickle cell disorder in our study. This is in contrast to mostfindings in published literature from other countries, where SCA is the commonest. Only one otherstudy conducted in eastern India, has depicted a finding similar to ours. The median age of disease presentation was at a later age in our study, in contrast to findings inpublished literature from other countries. There is a variation in the severity of disease manifestationin our study cohort. The most common painful crisis was bone pain, followed by abdominal pain.Pallor was also one of the commonest presenting symptoms. Stroke, a common manifestation of SCA in other countries, was rare in our study cohort.

63. **Clinical hematological and molecular characterization of sickle cell HbDpunjab (HBSD) in Eastern India: The largest series in world**

    2012

    Indian Journal of Hematology and Blood Transfusion

    Bishwal, S C and Patel, D K and Patel, S and Dehury, S and Purohit, P and Meher, S and Padhan, B and Das, K

    Introduction: Although HbDPunjab>b-121(GH4)Glu ? Gln] is the commonest haemoglobinopathy in northern India, HbSD, the compound heterozygote state with sickle gene is rare. Hereby we report detailed profile of 36 cases Hb SD, the largest number hitherto reported in world literature. Objectives: To describe the clinical, hematological and molecular profile of 36 HbSD patients from Eastern India. Materials and Methods: HbSD disease was diagnosed by HPLC. All cases were subjected to detailed clinical, radiological, biochemical examination and CBC. HbS mutation was confirmed by ARMS-PCR, HbDPunjab mutation was confirmed by EcoR1-RE digestion following PCR, RFLP and Xmnl polymorphism were studied by analyzing six RE sites as described by Orkin et.al (1982). a-Thalassaemia was diagnosed by GAP-PCR. Results: The mean age of patients was 21.63 Â± 11.7 years and majority belonged to a particular caste namely the Agharia, which is a predominant caste of Western Odisha. Highest number (30.55 %) of patients was from Sundergarh district. The commonest clinical presentation was blood transfusion (in 69.44 % of patients) followed by painful crisis (66.67 % of patients). 32.0 % of patients had splenomegaly and hepatomegaly. 18.18 %hadAVNof the femur head, 12.0 % had cholelithiasis, whereas 8.0 % had splenic atrophy. The mean Hb, MCV and MCH were 8.4 Â± 2.59 g/dL, 88.54 Â± 11.0 fl and 29.4 Â± 4.34 pg respectively in the HbSD patients. The mean HbF concentration was 19.05 Â± 9.95 % and HbD was 41.46 Â± 3.89 %. 81.18 % were heterozygote for Xmnl polymorphism whereas 18.82 % were homozygotes and 5 cases (15.0 %) had deletional a-thalassaemia. Conclusion: We report the detail profile of 36 cases of HbSD patients who were thoroughly investigated and their detailed molecular characterization was accomplished.

64. **Retraction notice to â€œGene frequency reports of sickle cell trait among six human populations of Jammu and Kashmir, Indiaâ€ [GENREP 4C (2016) 1â€“5] (Gene Reports (2016) 4 (1â€“5), (S245201441630005X), (10.1016/j.genrep.2016.02.003))**

    2020

    Gene Reports

    Fareed, M and Anwar, M A and Ahmad, M K and Afzal, M

    This article has been retracted: please see Elsevier Policy on Article Withdrawal (https://www.elsevier.com/about/our-business/policies/article-withdrawal). This article has been retracted at the request of the authors. The authors have informed the journal that in addition to numerous errors in the methodology, they now recognise that the experiments reported in this article were not repeated more than once

for validation and so are not statistically relevant. The authors therefore wish to retract this article so as not to mislead the scientific community.

65. Epidemiology of sickle cell disease in state of Chhattisgarh

2010

Indian Journal of Public Health Research and Development

Patra, P K and Tripathi, S and Khodiar, P and Sablania, P and Keshari, J R and Dalla, A R

Sickle cell disease (SCD) is the commonest abnormal hemoglobin in the world. The present study evaluated the SCD in state of Chhattisgarh. The study was conducted in Center for Genetic Diseases & Molecular Biology, Department of Biochemistry, Pt JNM Medical College & associated BRA Hospital, Raipur during the period of 4 years from May 2003 to April 2007. The screening was conducted on a total of 38472 individuals. We found that the prevalence of SCD in India is highest in the state of Chhattisgarh (23%). Though the prevalence is high for tribal and scheduled caste populations, the prevalence is highest for Kurmi (55%)and Teli (53%)caste which belong to backward castes. Solubility tests are highly sensitive and specific for detecting SCD & can easily be used for mass screening of SCD. The term SCD in the present study includes both sickle cell trait and homozygous sickle cell anemia.

66. Evaluation of lipid profile status in sickle cell disease patients of north maharashtra

2016

Biomedicine (India)

Jadhav, A J and Vaidya, S M and Bhagwat, V R and Dange, C D

Aim and Objective:The aim of this study was to evaluate the lipid profile status and atherogenic index of plasma in sickle cell patients in a steady state from the tribal population of North Maharashtra. Material & Methods: Thirty three sickle cell disease (HbSS) patients in the steady state, twenty six sickle cell carriers (HbAS) and thirty normal healthy volunteers with (HbAA) aged 18-40 years were recruited for the study. Subjects having past 3 months history of the vaso-occlussive crisis, blood transfusion and serious illness were excluded from the study. The lipid parameters were measured using enzymatic assay methods, while LDL-cholesterol was calculated by using the Friedewald's formula. Results:The mean plasma total cholesterol levels(TC), high-density lipoprotein cholesterol (HDLc) and low-density lipoprotein cholesterol (LDLc) in sickle cell disease patients were significantly decreased ($p<0.05$) when compared with the sickle cell carriers and the healthy controls. However the plasma triglyceride levels and very low-density lipoprotein cholesterol (VLDLc) were found to be significantly high ($p<0.05$) in sickle cell disease patients when compared with the sickle cell carriers and healthy controls. Atherogenic index of sickle cell patients is higher however not statistically significant when compared with the sickle cell carriers and the healthy controls. Conclusion:Low levels of TC, HDLc, LDLc and high levels of triglycerides and VLDLcwere found in sickle cell disease patients from North Maharashtra. Atherogenic index of plasma indicates the sickle cell disease patients are prone to develop atherosclerosis. The elevated serum triglycerides may often be a risk factor for various cardiovascular abnormalities including pulmonary hypertension.Their marked hypocholesterolemia should be a cause for concern about the overall mortality and general well-being. Dietary changes and lifestyle modifications are advised.

67. Prevalence of haemoglobinopathies in Western Rajasthan

2020

Indian Journal of Hematology and Blood Transfusion

Madhubala, R and Gupta, A K and Kumar, M and Saini, S and Purohit, A and Didel, S and Elhence, P and Singh, K

Aims & Objectives: Haemoglobinopathies encompass the most common autosomal recessive genetically inherited monogenic red blood cell disorder, globally caused due to point mutation or elimination of the Î±/Î²-globin genes resulting in abnormal globin chain synthesis. It has been estimated that in India 0.37 per 1,000 fetuses have Hb disorder. This is a retrospective observational study performed at AIIMS Jodhpur, to study the prevalence of haemoglobinopathies in western part of Rajasthan. Patients/Materials & Methods: All suspected case of haemoglobinopathies, from October 2017 to March 2020 were included in the study. Blood samples were collected in EDTA vials and analyzed with Sysmex XN1000 and peripheral blood smears were prepared. The haemoglobin HPLC for various haemoglobinopathies was performed on Biorad Variant D-10. Results: In this retrospective study, we studied a total of 1668 cases. The mean age of the patients coming for HPLC testing was 24.78 Â± 12.62 years with female preponderance of 4:1. On Hb-HPLC, 225(13.48%) cases revealed features of haemoglobinopathy while remaining 1443(86.52%) cases were normal. The most common Hb abnormality detected was Î² thalassemia trait present in 181 (10.85%) patients, followed by Hb D Punjab trait in 17 (1.01%) cases and b thalassemia major 13 (0.78%). One case (0.06%) of HbH, Eb thalassemia and and HbE disease and two cases (0.12%) of sickle-b thalassemia, sickle-cell disease and HbE trait were observed. Discussion & Conclusion: In the present study, the prevalence of Hb disorders was found to be 13.48%, and the most common Hb abnormality detected was that of b thalassemia trait (10.85%) which is in concordance with similar studies from other parts of the country. Hb-HPLC is a reliable investigation for the early detection and management of hemoglobinopathies and variants, in view of the high incidence of beta thalassemia trait in the Indian subcontinent. Moreover, knowledge of common Hb patterns in this particular region helps to formulate appropriate preventive and therapeutic strategies.

68. Comparison of haematological parameters in crisis and steady state in patients of sickle cell anaemia and trait

2012

Australasian Medical Journal

Priyadarshi, V M and Anshu

Introduction Sickle cell disease is characterised by severe haemolytic anaemia, chronic organ system damage and decrease in life expectancy. Sickle cell anaemia is the homozygous state and sickle cell trait is the heterozygous state for the HbS gene.Aims: This study was carried out to compare haematological parameters in patients of sickle cell anemia in crisis and steady state to determine if they can predict the onset of crises. Materials and Methods 85 cases with AS and SS pattern on haemoglobin electrophoresis were enrolled. The haematological parameters in both groups were compared. Results 67 patients had trait (AS) while, 18 had sickle cell disease (SS). 27 (31.8%) cases presented with some form of crisis, while 58 (68.2%) were in the steady state. 13 (72.2%) SS patients and 14 AS patients were in crisis. Hemoglobin, red cell counts and hematocrit of patients in crisis were significantly lower than those in steady state. Patients in vaso-occlusive crisis showed significantly higher number of granulocytes, platelets and platelet distribution width compared to patients in aplastic or haemolytic crisis. Total leukocyte and platelet counts of SS patients in crisis were significantly higher than those in steady state. Platelet distribution width of AS patients in crisis were significantly higher than those in steady state. Conclusions Haematological parameters cannot be used reliably to distinguish onset of a crisis in patients of sickle cell disease. However knowledge of baseline WBC and platelet counts can help in predicting severity and onset of vaso-occlusive crisis.

69. Gene frequency reports of sickle cell trait among six human populations of Jammu and Kashmir, India

2016

Gene Reports

Fareed, M and Anwar, M A and Ahmad, M K and Afzal, M

Sickle cell disease (SCD) is the most commonly inherited blood disorder, causing high child mortality worldwide. The study aimed to determine the prevalence and gene frequencies of sickle cell trait (SCT) among six regional human populations from Jammu province of Northern India. The prevalence of SCT ranged from 4.41% to 16.36%

among males and 6.67% to 20.83% among female children of six populations. The average prevalence of SCT was 9.30% observed among males and 11.16% among female children. The highest frequency of sickle cell trait was observed among Mughal population (male = 16.36%, female = 20.83% and combined group = 18.45%). The lowest frequency of sickle cell trait was found among Khan population (male = 4.41%, female = 6.67%, and combined group = 5.47%). The population-based chi-square values showed a significant difference ($p < 0.05$). We observed significant differences in the allele frequencies of SCT among six human populations. The results from this study provide information on the genetic variation of SCT among different human populations inhabiting Jammu and Kashmir. Understanding the epidemiology of SCT at population level would help in genetic counseling strategies to minimize its harmful consequences.

70. A novel symptomatic b0-thalassaemia mutation CD-15(-T) in compound heterozygote first time with sickle cell gene from Eastern India & response to hydroxyurea

2014

Indian Journal of Human Genetics

Meher, S and Patel, D K and Patel, S and Das, K and Dehury, S and Purohit, P and Jana, A and Bhattacharya, S and Mohanty, P K and Sarkar, B

Background The HbS and Î²-thalassaemia genes are common hameoglobinopathies with variable prevalence in India. Like HbS homozygotes, HbS-Î²-thalassaemia also shows severe clinical presentation. Odisha state is having a high prevalence of these genes. This is the first report of two cases with a novel Î²0-thalassaemia mutation (codon 15, TGG>-GG;del T) co-inherited with HbS with severe clinical symptoms of repeated VOC, BT, Hosp. Aim and objective Molecular characterizations of HbSÎ²0 thalassaemia and response to HU therapy. Material & method Standard laboratory investigations confirming HbS and Î²-thalassaemia were adopted. CE-HPLC was done to quantify hemoglobin fractions. PCR-ARMS was adopted to confirm known mutations and direct Î² globin gene sequencing was done to identify rare mutations. CBC and Biochemical investigations, Radiological examination of shoulder and Hip joints, USG of abdomen were done to correlate clinical findings. Hydroxyurea (HU) was administered at a low and fixed dose (10 mg/kg/day) based on indications. Result Both the 2 cases of HbS-Î²-thalassaemia with codon 15 (-T) mutation had repeated VOC, BT, Hosp as the presenting symptom at 2 and 3 yr of age respectively. CBC agreed to typical thalassaemic red cell picture (MCV 66.9Â±1.8, MCH 19.7Â±0.42) with high HbA2 (6.75Â±1.4) in CE-HPLC. The cases were confirmed to be HbS-Î²0-thalassaemia with a novel Î²-thalassaemia mutation at codon 15, TGG>-GG; del T by direct globin gene sequencing. The patients were treated with Hydroxyurea (HU) and are under regular follow up since 2 yr with 100% response. Conclusion All HbS-Î²-thalassaemia are not symptomatic but this novel Î²0 thalassemia when coinheried with HbS showed clinical manifestation. Hydroxyurea has been a drug of choice for the SCD patients. It responds well and effective even at a low dose of 10 mg/kg/day and can be administered this drugs to cases of HbS-Î²0 Thalassaemia patients.

71. Haemoglobin S and Î²Thal: Their distribution in Maharashtra, India

2013

International Journal of Biomedical Science

Urade, B P

It has been more than six decades since the first report of sickle cell anaemia in Indian subcontinent. Since then the researchers have been reported various haemoglobin varients prevalent in India, they are HbS, HbÎ²T, HbE and HbD. Earlier studies were confined to tribal and scheduled castes populations as if sickle haemoglobin was restricted to these two groups only. Since a decade or so, few studies on haemoglobinopathies from other Indian populations are available. Examination of premarital age group of 5172 Indian subjects (2762 males and 2410 females) from eastern Maharashtra of India showed high incidences of HbS (0-33 per cent) and HbÎ²T (0-10 per cent) in different ethnic groups. In present study cumulative gene frequency for HbS and HbÎ²T was found to be of 6.1 per cent and 2.3 per cent respectively. In present study sickle cell gene has been found in general categories of Indian populations besides scheduled castes and tribal populations. In Scheduled tribes HbS ranges from 0-24 per cent, in Scheduled castes and Nomadic tribal groups, HbS ranges from 0-13 per cent, in Other Backward caste categories it varies from 0-20 per cent while in higher caste populations it ranges from 0-5 per cent. The incidences of HbS are much higher among tribal groups than that found in other caste populations. The incidences of

homozygous individuals are very few in HbS and HbÎ²T. The hitherto regional and populations specific HbÎ²T haemoglobin variant in Sindhi and Bengali communities is gradually spreading in other populations of Maharashtra as evident from the present study. Lesser value of MCV, MCH and MCHC in homozygous HbÎ²T is due to impairments of synthesis Î²-globin chain. The subject with the presence of Î²-thalassaemia is accompanied by raised level of HbA2. Unusual higher values of RBC and WBC suggest the high concentration of hypochromic microcytosis in anemia. The means of MCV MCH and MCHC in HbÎ²T are much lower than the normal ranges compared to HbS. Â© 2013 B. P. Urade.

72. Genetic counseling an essential component of thalassemia management for mitigating disease burden

2014

Indian Journal of Human Genetics

Iyer, G R and Pujar, A and Jalal, T and Salma, B U and Poornima, S and Jain, S and Hasan, Q

Background: Beta-thalassemia is a type of hemoglobinopathy wherein the body fails to produce enough hemoglobin leading to decreased oxygen supply to the organs causing life threatening problems. It follows autosomal recessive mode of inheritance requiring both the copies of the gene to be nonfunctional to cause the disease. Thalassemia and Sickle Cell Society (TSCS) in Hyderabad is a referral center where the patients from different parts of Telangana, Andhra and Maharastra-Karnataka border come for subsidized transfusion and chelating drug therapy. Aims & Objectives: To evaluate the problems faced by families with a child affected with thalassemia and the role genetic counseling plays in creating awareness to mitigate the burden of this disease both at the family and community level. Materials & Methods: 151 Families at TSCS were randomly interviewed during the transfusion session of their child. Details were recorded in a well designed proforma about the clinical, financial and social factors associated with diagnosis and treatment of their child. Results: In only 39% of the cases the primary health care provider diagnosed Beta-thalassemia, while in the majority of the cases, especially from smaller districts, the families had to travel to Hyderabad for diagnosis and still travel for transfusions monthly once/twice.. Most of the cases were diagnosed between the ages of 3months to 5 years. Contrary to popular belief 46% of the cases were born to non-consanguineous couples. 14% of the patients had an older sib with thalasemia. Conclusions The study revealed that primary care physicians require training to diagnose thalasemia. TSCS can train personnel so that sub-centres can be set-up in districts for management of the disease. Appropriate genetic counseling should be given for preventing recurrence of the disease in the same family especially by promoting extended family screening and appropriate pre-natal testing. Effective Government policies need to be introduced to mitigate the burden of this disease in our population.

73. Burden of hemoglobinopathies in malwa region: A retrospective study

2020

Indian Journal of Hematology and Blood Transfusion

Singh, U and Saxena, P

Aims & Objectives: To find the type of hemoglobinopathies in cases who presented with microcytic hypochromic anemia. Patients/Materials & Methods: The study was conducted on 517 individuals attending the OPD of a tertiary care centre between June 2018 to March 2020 with microcytic hypochromic anemia on routine CBC & peripheral smear. Sickling test was conducted and subsequently all these cases were subjected to Hemoglobin electrophoresis. Results: 178 out of the total of 517 (34.4%) cases were found to have one or the other form of hemoglobinopathy. Out of 178 cases 34.3% cases were of Sickle cell anemia, 29.8% cases of Beta thalassemia, 20.8% cases of sickle cell Trait and 15.2% cases of sickle-beta thalassemia. Rest i.e. 339 (65.6%) were subjected to further investigations like iron studies and revealed a mix of Iron Deficiency Anemia (80.5%) and anemia of chronic disease (19.5%). Discussion & Conclusion: Sickle Cell disorders has wide spread presence in different tribes of Central India. To reduce the burden of hemoglobinopathies screening of all anemic patients should be

done in all areas and in all communities where the socioeconomic condition indicate frequent occurrence of genetic mutations.

74. Molecular characterization and influence of Î±Î±/-Î±3.7 deletion on hematological and clinical heterogeneity of sickle beta 0 thalassemia in western Orissa, India

2009

Indian Journal of Hematology and Blood Transfusion

Dash, P M and Patel, D K and Patel, S and Mashon, R S

Background: Heterogeneity in clinical manifestation of Sickle Beta Thalassemia (SÎ²-Thal) may occur from nature of beta-thal mutation. In Western Orissa, India the SÎ²0-Thal patients with similar Î² thal mutation (IVS1-5Gâ†'C) are presenting with variable clinical severity. Aim: To determine the Î² globin cluster haplotype, coinheritance of alpha thalassemia and Xmn-I polymorphism; and to assess the impact of these genetic determinants on the phenotypic variability in SÎ²0-Thal subjects. Methodology: The study was conducted at Sickle cell Clinic, V.S.S. Medical College, Burla, Orissa. Detailed clinical and hematological parameters were studied in 45 SÎ²0-Thal [Î²S/Î²Th IVS1-5(Gâ†'C)] patients with informed consent. PCR analysis (RFLP, MULTIPLEX) were done to characterize the Î² globin cluster haplotype (Hinc-II, HindIII G and Î³A, Hinc-II Î¨Î², and 3â€²IIÎ², Ava-IIÎ², Hinf-I 5â€²Î²), co-inheritance of alpha thalassemia (3.7 and 4.2kb deletions) and Xmn-I polymorphism. Clinical severity was evaluated on the basis of pain rate (VOC/pt/Yr), frequency of hospitalizations, blood transfusion (BT/pt/Yr) and spleen size (ultrasonography). The clinical severity was correlated with hematological indices (Hb, MCV, HbA2, HbF, HbS), Î² globin cluster haplotype, alpha thalassemia and Xmn-I polymorphism. Statistical analyses were done using t-test and correlation analysis. Result: IVS1-5(Gâ†'C) mutation was strongly linked with single Î²S Asian haplotype (++-+++-) & multiple Î²Th haplotype (+ - +, - +, -). The overall frequency of single alpha chain deletion was 30% in the SÎ²0-Thal subjects (Î±Î±/-Î±3.7 in 28% cases & Î±Î±/-Î±4.2 in a lone case) and Xmn-I polymorphism was seen in all the cases (+/+ in 11% and +/- in 89%). Discussion: Patients with Î±Î±/-Î±3.7 deletion were clinically less symptomatic (decrease in pain and transfusion rate) with significant decrease in HbS ($p<0.05$) and an increase in HbF value ($p<0.05$) regardless of beta globin cluster haplotype and Xmn-I polymorphism, whereas frequency of hospitalization and spleen size were similar.

75. Comparison of Cephalic index of three states of India

2012

International Journal of Pharma and Bio Sciences

Gujaria, I J and Salve, V M

Cephalic index is the ratio of the maximum breadth of head to its maximum length. cephalic index is very useful anthropologically to find out racial differences. It has also been reported that cephalic index is less than 2-3 in individual with sickle cell anemia than normal individual. Materials and Methods: The present study was carried out at three places Mumbai (Maharashtra), Chinnaoutpalli (Andhra Pradesh) and Ahmedabad (Gujarat). This study was carried on 440 (220 male & 220 female), 420 (210 male & 210 female), 500 (302 male & 198 female) medical students of Mumbai, Chinnaoutpalli and Ahmedabad respectively. Results: The mean cephalic index for Maharashtra populationwas 78.14. The mean cephalic index for Andhra Pradesh population was 77.32. The mean cephalic index for Gujarat population was 80.81. Discussion & conclusion: The result of present study shows that cephalic index of Maharashtra population is almost 1 point higher than Andhra Pradesh population. In Maharashtra and Andhra Pradesh population cephalic index of the female is almost 2 points higher than the male. This study will serve as a basis of comparison for future studies on Maharashtra, Andhra Pradesh and Gujarat population.

76. Epidemiology of beta thalassemia trait in western Odisha

2012

Indian Journal of Hematology and Blood Transfusion

Meher, S and Patel, D K and Patel, S and Purohit, P and Dehury, S and Bishwal, S C and Padhan, B and Das, K

Introduction: Heterozygote state of Beta thalassaemia (Beta thalassaemia trait or BTT) is benign and asymptomatic. Detection of BTT has been very important in the effort of prevention of the disease by prenatal diagnosis. Microcytic hypochromic red cells and an elevated HbA2 fraction is hallmark to detect BTT. Objective: To study the epidemiology of BTT in Western Odisha from our Centre. Material and Method: Total of 5690 blood samples were collected from cross sectional study from different parts of Western Odisha were studied at the Sickle Cell Clinic and Molecular Biology Laboratory, V.S.S. Medical College, Burla, Odisha, India. Samples were subjected to CBC and CE-HPLC to quantify haemoglobin fractions. Cases with MCV<80 fl and MCH<27 pg were suspected for BTT (Colah et al. 2007). Cases with HbA2>3.5 % (Madan et al. 2010) and HbF<3.0 % were considered as BTT. Results: From a total of 5690 cases, 213 (3.7 %) individuals were found with BTT. The mean age of males and females were 32.1 Â± 14.1 and 31.7 Â± 14.6 years respectively. 3 (1.16 %) cases of BTT were found among a total of 259 ANC cases screened. 97.65 % of BTT were Hindu by religion and only 2.35 % were from other religions. Among Hindus, 44.6 % fall under OBC and 24.9 % under SC category, whereas 30 cases each were from ST and general category. While BTT was found preponderant among individuals from various districts of Odisha; Cases of BTT were also detected in individuals from West Bengal, Chhattisgarh and Andhra Pradesh. Conclusion: The prevalence of beta thalassemia gene in Western Odisha was 3.7 %. The finding that the religious groups like Muslims and Christians have lower frequency of BTT differs from the observation (Sur and Mukhopadhyay 2006) from West Bengal. The trend observed in this study though is unique in its representation of epidemiology of BTT from Eastern India; a larger population-based investigation is required to map the spread of Î²-thalassaemia gene in Eastern India.

77. Donor lymphocyte infusion in children-efficacy in preventing graft rejection and relapse-experience from a tertiary referral centre in southern India

2018

Indian Journal of Hematology and Blood Transfusion

Venkateswaran, V S and Meena, S and Shivani, P and Kesavan, M R and Nikila and Ramya, U and Lakshmanan, V and Revathi, R

Background: Donor lymphocyte infusion (DLI) is a form of cellular immunotherapy. In malignancies, it may be effective in preventing a relapse due to graft versus leukaemia effect and in benign hematological conditions it helps prevent the progression of impending graft rejection. There is scant data for the use of DLI in children and we describe the indications and cost effective methods of delivering care at our centre. Patients and methods: We conducted a retrospective analysis of the children who underwent hematopeitic stem cell transplantation and received donor lymphocyte infusion either as a part of pre-emptive therapy in leukaemia or for mixed chimerism in benign disorders at Apollo Cancer Institutes from the year January 2011 to May 2018. The first step was withdrawal of immunosuppression and DLI was commenced 7 days later if there was no evidence of graft versus host disease. The desired volume of fresh peripheral blood from the donor was infused based on the CD3 count. Donor lymphocyte infusion was given in a graded regimen with the cell dose of 1 x 10âˆ—5 CD3 cells/kg, 5 x 10âˆ—5 cD3 cells/kg, 1 x 10âˆ—6 CD3 cells/kg depending on the graft kinetics and the clinical status of the children. The dose was one log lower in children undergoing haploidentical HSCT starting at 1x10âˆ—4/kg. Results: A total of 569 children underwent HSCT during the study period and DLI was performed in fifty seven children. The male female ratio was 1.4: 1 and 72.4% were for benign haematological conditions including thalassaemia major, sickle cell anaemia and primary immune deficiency disorders. Reduced intensity conditioning was used in 12% children. The donor was a fully matched family donor in 90%, mismatch family donor in 6%, matched unrelated donor in 4%. A haploidentical family donor was used in 12%. Peripheral blood stem cells was

the stem cell source in 62% and bone marrow in 38% children. DLI was commenced for mixed chimerism less than 95% to prevent graft rejection in 79% and in 21% children it was used as pre-emptive therapy in high risk malignancies to prevent a molecular relapse. In our cohort, 26 children (45%) received single DLI, 17 (29%) received two DLI and three DLI was done in 13 children. In the majority of the children (72%), small aliquots of peripheral blood could prevent graft rejection / relapse. Twenty one children (46%) achieved 100% chimerism, 12 children (26%) had mixed chimerism and were clinically stable. Twenty two children who received DLI developed mild graft versus host disease of the skin and mouth and gut involvement was seen only in 4 of these children. The mortality was 17% (10/58) due to graft loss, relapse of leukemia and one death attributed to graft versus host disease. Conclusion: Donor lymphocyte infusion is an effective tool in children and helps prevent graft rejection in benign conditions and relapse of leukemia in high risk cases. It is a safe procedure for the donor as the graded regimen required very small amounts of peripheral blood from 0.1 ml to 75 ml. Careful follow up of graft kinetics and clinical vigilance for grade 4 graft versus host disease makes it an easily applicable tool even in resource constrained settings and in haploidentical HSCT.

78. Thalassemias: Can we reduce the national burden?

2014

Molecular Cytogenetics

Colah, R

The burden of inherited disorders of hemoglobin, the commonest group of single gene disorders in India is huge. With a population of 1.21 billion and an average prevalence of b-thalassemia carriers being around 3.5-4%, there would be 35-45 million carriers and the estimated number of births of affected babies annually would be 10,000-12,000. The carrier rates vary from 1-17% in different ethnic groups. Apart from b-thalassemia, Hb E is common in the north eastern region and in West Bengal (4 to > 50%) and Hb S is prevalent in parts of central, western and eastern India (5-40%). Thus interaction of the b-thalassemias with these Hb variants is not uncommon and can lead to a severe disorder. One way to combat the burden is by prenatal diagnosis but the only approach to reduce the national burden is by a comprehensive community control programme. Awareness is very limited in different states (<20% among pregnant women) and the entire public health infrastructure from medical colleges to district hospitals and down to the community health centres must be mobilized for education and generating awareness on these disorders. Experience shows that screening for carriers in India will have to be done at multiple levels-schools, colleges, antenatal clinics as well as cascade screening where extended family members of an affected child are screened. However, antenatal screening with subsequent testing of the husbands of carrier women would be the most cost effective way to identify couples at-risk and give them the option of prenatal diagnosis. For this, obstetricians must recognize the implications of hypochronic and microcytic red cell indices (MCV <80 fl, MCH < 27 pg and a high RBC count) and ask for a b-thalassemia screen by estimation of HbA2 levels. Several laboratories in the country use automated HPLC for reliable HbA2 estimation and identification of heterozygotes is not a problem. Late registration at antenatal clinics (only 15-20% in the first trimester in public hospitals) is an impediment resulting in many couples at-risk being identified late and requiring second trimester fetal diagnosis. Social stigmatization is an issue to be dealt with during premarital screening of marriage partners of carrier individuals. Only education can reduce this barrier. Many State Governments in India are now undertaking population screening and counselling programmes and Gujarat and West Bengal have taken the lead. There are 10-12 centres offering prenatal diagnosis by CVS and DNA analysis and recently the Indian Council of Medical Research has established 6 more centres in different regions. However, many more centres would be required once there is an increasing demand. The spectrum of mutations and their distribution are now known which would facilitate prenatal diagnosis. Thus, there are many challenges-a large and diverse population, limited awareness, late registration in antenatal clinics and inequality of available services (urban v/s rural areas) with around 70% of the population residing in rural areas. There is a need for the Central and State Governments to join hands and involve NGO groups to form networks in different regions which when backed by political will could gradually reduce the national burden of hemoglobinopathies in this vast country.

79. Global estimates of sickle hemoglobin in newborns

2011

American Journal of Tropical Medicine and Hygiene

Piel, F B and Patil, A P and Howes, R E and Nyangiri, O A and Gething, P W and Dewi, M and Temperley, W H and Williams, T N and Weatherall, D J and Hay, S I

Reliable estimates of the populations affected by medical conditions are necessary to guide effcient allocation of resources in public health. Despite sickle cell disease being the most common haemoglobinopathy globally, up-to-date estimates of the populations affected are lacking. Moreover, only national estimates of heterozygous (AS) and homozygous (SS) newborns have been published and their precision is not known. Using a georeferenced database of sickle haemoglobin (HbS) surveys, a contemporary evidence-based global map of HbS allele frequency distribution was created within a Bayesian model-based geostatistical framework. This map illustrates strong sub-national spatial heterogeneities and shows high allele frequencies across most of sub-Saharan Africa, the Middle East and India, as well as in areas where the gene spread following human migrations (rather than selection), in Western Europe and along the eastern coast of the Americas. The pairing of predicted HbS allele frequencies with high spatial resolution population counts for 2010 and national crude birth rates enabled calculation of global, regional, national and sub-national estimates of the annual number of AS and SS newborns. The uncertainty in these estimates was calculated using sampling of the allele frequency posterior predictive distributions. In many low- and middle-income countries, the epidemiological transition has greatly reduced infant and child mortality, and improved the survival prospects of HbS patients. In most high-income countries, the need for appropriate diagnoses and genetic counselling to control the number of newborns affected and reduce the risk of complications, as well as the economic burden of treatment and hospitalization, has become more evident. Globally, this situation results in an increasing impact of HbS on public health systems. By taking into account local heterogeneities in HbS allele frequencies and providing uncertainty measures, the maps and estimates presented here provide key spatial intelligence on our current knowledge at various scales and defne areas most in need of further research.

80. Relation between the uridine diphosphate glucuronosyltransferase 1A1 polymorphism and the bilirubin levels in sickle cell disease

2012

Journal of Clinical and Diagnostic Research

Pandey, S and Ranjan, R and Firdos, A and Shah, V and Pandey, S W and Mishra, R M and Seth, T and Saxena, R

Background: Genetic variations in the promoter of uridine diphosphate (UDP)-glucuronosyltransferase 1A1 (UGT1A1) may be associated with hyperbilirubinaemia and it appears to be a risk factor for gallstone formation. Aims: Our aim was to detect the correlation between the UGT 1A1 (TA)n repeats and hyperbilirubinaemia and gall stone formation in Indian sickle cell patients. Settings and Design:This was a cross-sectional study; which was carried in an autonomous tertiary care hospital. Materials and Methods: The study subjects were 50 sickle cell anaemia and 70 sickle cell Î²-thalassaemia patients who were diagnosed by HPLC. The haemogram of the patients was measured by using an automated cell analyzer, while the serum bilrubin measurement was done by using a Beckman- CX-9 auto analyzer. The presence of gall stones was detected by ultra sound examination. Statistical Analysis: ANOVA and the T-test were applied to compare the means of the groups. The allele frequencies were calculated according to the Hardy-Weinberg equilibrium. Results: The allele, 7/7 TA of the UGT1A1 genotype was more frequent in the sickle cell patients and it was associated with hyperbilirubinaemia and gall stone formation. Conclusions: The allele, 7/7 TA of the UGT1A1 polymorphism affects the bilirubin levels and the development of gallbladder stone in the Indian sickle cell patients.

81. Influence of Î± thalassemia on the protective effect of sickle cell gene on severity of P. Falciparum malaria

2016

International Journal of Infectious Diseases

Purohit, P and Patel, S and Mohanty, P K

Background: P. falciparum malaria and sickle-cell-anemia are two major public health problems in western Odisha. It has been hypothesized that sickle-cell-gene protects against severe P. falciparum malaria. Again, African studies described the negative epistatic interaction for protection against malaria between sicklecell- gene and Î±-thalassemia when co-inherited together. This study was undertaken to assess the role of Î±-thalassemia on the protective effect of sickle-cell-gene on severe P. falciparum malaria. Methods & Materials: Adults patients with severe P. falciparum malaria were included. Age, sex and ethnic matched control (no malarial infection since 5 years) were taken. Sickle-cell-gene and Î±-thalassemia was confirmed by ARMS-PCR and GAP-PCR respectively. Clinical and haematological data were analyzed. Results: 396 patients were registered, including 284, 66 and 46 patients with HbAA, HbAS and HbSS respectively. In control (total 391 cases), 301 cases had HbAA and 90 cases had HbAS. In HbAA with severe falciparum malaria, the incidence of Î±-thalassemia was 36.6% (104/284) in patients compared to 47.2% (142/301) in control (Ï‡2,6.25; p=0.012). In HbAS, the incidence of Î±-thalassemia was 81.8% (54/66) in patients compared to 52.2% (47/90) in control (Ï‡2,13.3; p=0.0003). In HbSS, the incidence of Î±-thalassemia was 63.0% (29/46). In HbAA, patients with Î±-thalassemia had increased Hb and RBC levels with lowered MCV and MCH compared to normal Î±-genotype. In HbAA, the incidence of ARF, Jaundice, cerebral malaria and death were significantly low in patients with Î±-thalassemia. The number of complications has increased with decreased Î±-globin gene number in both patients with HbAS and HbSS. In HbAS, patients with Î±-thalassemia had a greater HbA/HbS ratio compared to patients with normal Î±-genotype ($p<0.01$). Conclusion: Patients with Î±-thalassemia had better haematological and clinical parameters compared to normal Î±-genotype in HbAA. The high incidence of Î±-thalassemia in patients with HbAS, suggest the negative epistatic interaction of Î±-thalassemia on the protective effect of HbAS against severe malaria. This hypothesis again supported by high HbA/HbS ratio in our patients with HbAS and Î±-thalassemia. Longitudinal cohort study is essential to understand the pathophysiology of malaria and haemoglobin disorders in India.

82. Putative pathogenic effect of oxidative stress in sickle cell disorder

2011

Biomedical Research

Goswami, K and Ray, D

Sickle cell disorder is a major hemoglobinopathy associated with hemolytic anemia. It mani-fests either as less severe heterozygous or severe homozygous form. Evidences suggest in-volvement of oxidative stress in this disorder. Hence we made an attempt to find out any pa-thogenic impact of oxidative stress in this disease. From the rural area of central India 80 heterozygous and 20 homozygous cases were registered as two separate groups. Along with this 100 and 66 age and sex matched healthy individuals were included as controls against these two groups of cases respectively. Malondialdehyde and superoxide dismutase activity in serum and catalase activity in erythrocytes were assayed as markers of oxidative stress. Hemoglobin level and reticulocyte count were measured to assess the severity of hemolysis. Statistical comparisons were made between cases and corresponding control levels for all these parameters. Also study was done to find any association between oxidative and hema-tological parameters.The result showed overall oxidative and hemolytic stress in both group of cases. However, except for malondialdehyde which showed significant increase in both the forms of the disease, all other parameters studied showed significant difference only in homozygous but not in heterozygous cases. Also significant association between oxidative parameters and hematological response was recorded only in homozygous cases. Finally li-pid peroxidation was found to be the strongest predictor variable for hemolytic stress re-sponse. Results indicate association of oxidative pathology with the severe form of this dis-order and advocate oxidative damage as the putative pathogenic determinant in this disor-der.

83. Hemoglobinopathy: Spectrum and effects of coexisting nutritional deficiency

2016

Indian Journal of Hematology and Blood Transfusion

Nayar, S and Acharya, S and Kishore, S and Acharya, R

Introduction and Background: India is a significant reservoir of b thalassemia and allelomorphs of HbbA with variable geographical distribution. This study was undertaken to find out the spectrum of hemoglobinopathies by CE HPLC in local population, to evaluate the haematological parameters in these cases and to evaluate effects of nutritional deficiency on HbA2 levels. Patient/Material and Methods: In this prospective study conducted on 2197 samples, RBC indices were obtained by Sysmex XP 100 and CE HPLC was performed on BIORAD D10. The variant hemoglobins were identified on the basis of their percentage, retention times and peak characteristics. PBF, reticulocyte count, HbH inclusion and sickling test were done in selected cases. Serum ferritin was assayed in 139 cases by chemiluminescence. Megaloblastic anemia was diagnosed by CBC and PBF with bone marrow examination/vitamin B12 levels in a few cases. Statistical analysis was done using Student t test. Results: Hemoglobinopathies was seen in 5.28 % cases. Heterozygous and homozygous Î² thalassemia comprised 3.27 % and 0.18 % of total cases respectively. 2 % variant hemoglobins (46/2197) included HbD trait (21), HbE trait and disease (12), HbS trait (06), HbQ India (02), HbD Iran (02), HbJ Meerut (01) and HbH (02). Four cases were compound heterozygous. A presumptive diagnosis of Î± thalassemia was made in 49.2 % (32/65) of cases. Coexisting iron and vitamin B12 deficiency was seen in 27.27 % (6/22) and 8.3 % (6/72) of Î² thalassemia traits respectively. Mean HbA2 levels was higher in megaloblastic anemia and lower in iron deficiency anemia in cases with normal HPLC pattern ($p<0.05$). Conclusion: Antenatal screening for hemoglobinopathies is recommended using CE HPLC. Coexisting nutritional deficiency alters HbA2 level significantly.

84. Prevalence of thalassemia in west bengal with special reference to different tribes

2012

Indian Journal of Hematology and Blood Transfusion

Basak, J and Bhattacharyya, D M and Mukhopadhyay, S and Dasgupta, S and Chakraborty, A and Das, P and Pal, N and Koner, S and Mukhopadhyay, A

Introduction: Thalassemia is a hereditary anemia resulting from defect in hemoglobin production and it is the most common genetic disorder worldwide. Prevalence of Thalassemia (both alpha and beta) is high in West Bengal, especially among the scheduled tribes. To reduce the Thalassemia burden from West Bengal we have taken a project for Thalassemia carrier screening through awareness and screening program among the rural and urban populations. Our target population were tribes, e.g., Toto, Rabha, Munda, Oraon, Kerketa, Sardar etc. residing in remote rural areas. Materials and Methods: From January 2009 to December 2011, we have organized 73 camps in different districts of West Bengal. After taking written consent, 2-3 ml peripheral blood samples were collected from each interested people attending the mass awareness camp. NESTROF, CBC, HPLC were done for all samples. To detect alpha and beta mutations GAPPCR and ARMS-PCR were performed following the standard protocol. Results: During the above mentioned period, we have screened on total 8387 individuals (4,869 male; 3,518 female) for Thalassemia carrier detection through camps, organized in 14 districts of West Bengal. Out of 8,387 screened individuals, tribes were 2,885 and general caste including scheduled castes was 5502. Among tribes HbE carrier and homozygous percentage are 14.6 and 4.01 respectively while percentage of sickle cell anemia and beta Thalassemia carriers are 1.25 and 4.19 respectively. Total beta carrier percentage among general caste and scheduled caste is 6.94. Our result also revealed that alpha Thalassemia carrier among Oraon and Sardar tribes is very high. Conclusion: Incidence of Thalassemia is high in different rural populations especially among tribes. So, large scale awareness and preventive program should be taken.

85. Prevalence of thalassemia syndromes, hemoglobinopathies and mutation analysis in a tribal school in India

2019

Leukemia Research

Oberoi, A and Kanakia, S

Objective: To detect the prevalence of Thalassemia Syndromes and Sickle Cell Anemia in a tribal school population of adolescent age group and Mutation Analysis of the positive cases. Background: Thalassemia and other hemoglobinopathies are the most common monogenic disorders in India with a high prevalence in tribal populations. Social stigmas, difficult living terrains and high cost of treatment makes the management of such disorders difficult in the study population. Methodology: This study was conducted on 211 children aged 10â€“14 years from a tribal school in the state of Maharashtra, India. After taking clinical history, complete hemogram report was obtained by an automated cell counter. High-performance liquid chromatography (HPLC) was performed on the samples with Bio Rad D-10â„¢ Analyser. The samples with abnormal electrophoresis patterns were subjected to Next Generation Sequencing of HBH gene for mutation analysis. Results: Of the 211 students sampled, 193 (91.5%) had a normal electrophoresis pattern and abnormalities were detected in 18 (8.5%) cases. Î² (beta) thalassemia trait was the commonest abnormality found in 16 (7.6%) children. Heterozygous Sickle Cell and Alpha Thalassemia were found in 1 (0.5%) case each. Of the 16 Thalassemia traits, 13 (81.25%) had IVS1-5(G>C) mutation, followed by c.47G>A (p. Trp16Ter) in 2 students (12.5%) and IVS1-1(G>T) c.92+1G>T in 1student (6.25%). The one sickle heterozygote had c.20A>T (p.Glu7Val) mutation. Conclusion: High frequencies of these mutant alleles are maintained by the tribal populations probably due to consanguinity, lack of awareness and conveyance; low income status and high cost of treatment make them vulnerable. These groups must undergo premarital screening to decrease the risk bearing offspring with hemoglobinopathies.

86. Prevalence of cardiovascular abnormalities and biochemical changes in sickle cell nephropathy patients -A study from tribal area (central India)

2010

Nephrology

Gupta, P and Gharote, M and Bodele, T and Gupta, G and Abraham, G

Introduction: We studied Various Biochemical changes and cardiovascular abnormalities that are present in sickle cell nephropathy patients from tribal areas. Methods: 37 patients of sickle cell nephropathy admitted in Dr.B.R.A.M Hospital Raipur were subjected to Serum proteins, Thyroid profile, Lipid profile, Hemoglobin electrophoresis, Electrocardiography, Echocardiography, and Renal Ultrasonography and Routine investigations. Results: â€¢27% were Males and 73% Females. Most of the patients were of age group 15-25 yrs. â€¢24.3% belonged to Utkal caste, 14.6% were Sahu, Panika 14.6%, and 21.9% of kurmi caste, others were 24.6%. â€¢Mean serum urea was 57 Â± 14 mg/dl and serum creatinine was 2.8 Â± 1.4 mg/dl. â€¢86.5% were anaemic (Hemoglobin <10 gm/dl). â€¢86% were having either one or more form of hematuria, pyuria, proteinuria. â€¢Mean 24 hr urinary albumin was1.5 Â± 0.5 gm/24 hr. Low serum albumin (<3 mg/dl) was present in 27.2% (p value < 0.0001). â€¢Hyponatremia was seen in 10.8%, hypokalemia in 21.6%, hypercalcemia 13.5%, hyperphosphatemia in 16.25%. Hypothyroidism in 2.7%. â€¢Dyslipidemia in the form of Hypercholesterolemia in 51.3%, hypertriglyceridemia in 5.4%. â€¢Sonography finding showed bilateral medical renal disease in 10.8%. â€¢ECHO finding was LVH was seen in 10.8%, valvular lesions in 9.3%. Conclusion: â€¢Most of patients were of 15-25 years. Maximum numbers of patient with sickle cell nephropathy were female. Sickle cell nephropathy was commoner in Utkal and kurmi caste. â€¢Most of the patients with Sickle cell nephropathy were anaemic. â€¢Maximum number of patients had abnormal urinary finding. â€¢Hypokalemia and hyperphosphatemia were common electrolyte abnormality in Sickle cell nephropathy patients. Hypercholesterolemia was most common lipid abnormality seen. â€¢LVH and Valvular lesions were Commonest cardiac abnormalities found in sickle cell nephropathy.

87. Sickle cell disease and pregnancy

2013

Indian Journal of Hematology and Blood Transfusion

Junagade, P

Introduction Sickle cell disease (SCD) and its heterozygous variants are common in our country. This inherited disease occurs in tribal population and in those with poor socio economic condition, often with limited or poor access to healthcare. Pregnancy brings with it a host of problems, most significant being anaemia. Anaemia is most likely due to iron deficiency, though other nutritional deficiencies are known. Sickle cell anaemia needs special attention especially in pregnant females. Although most pregnancies complicated by maternal SCD are likely to result in livebirth, these pregnancies are at increased risk of obstetrical and foetal complications, as well as medical complications of SCD. These risks are due, at least in part, to the metabolic demands, hypercoagulable state, and vascular stasis associated with pregnancy [1] A. Pre Conception Stage: 1. Testing partner for haemoglobinopathy. The risk of SCD in offspring is 50 % if the biologic father is heterozygous; the risk is 100 % if he is homozygous. If the partner has thalassaemia minor or sickle cell trait, then prenatal diagnosis can be offered to the patient. There are many social issues in India regarding â€œwho is responsible for the diseaseâ€ and hence should be handled extremely cautiously. 2. Prepregnancy evaluation: The patient's clinical history of pain events and hospitalizations should be reviewed. This evaluation should include: â€¢ Confirmation of definitive diagnosis: this is important as previous reports might be done on poor sampling and with old techniques. â€¢ Measurement of baseline blood pressure, since hypertension may be due to sickle nephropathy and is a risk factor for stroke and development of superimposed preeclampsia. â€¢ Retinal evaluation to detect early proliferative sickle retinopathy, which may worsen during pregnancy. â€¢ Chemistry panel, urinalysis, and 24-h protein excretion to determine baseline organ function, particularly sickle nephropathy. Knowledge of baseline parameters is important because both pregnancy and preeclampsia (which is common in SCD patients) may worsen renal function. â€¢ Haemoglobin and ferritin level. Women with SCD often have excessive iron stores, but a small proportion is iron deficient. Women with excessive iron stores should not receive vitamins with iron and should consider delaying pregnancy until they have been treated. It is common in our country to prescribe oral iron for every patient. â€¢ Baseline pulmonary function tests, including pulse oximetry, are recommended because of the increased risk of pulmonary embolism, acute chest syndrome in pregnancy. â€¢ Hepatitis B and C screening to assess risk of perinatal transmission. â€¢ Echocardiogram as a screening test for pulmonary hypertension and early cardiac dysfunction, which are associated with increased mortality in SCD and pregnancy. â€¢ Red cell genotyping and screening for red cell alloimmunization to identify patients with multiple red cell alloantibodies who may be difficult to match for transfusion and may be at risk for haemolytic disease of the foetus and newborn. This is not available in most centres, but an effort should be made to get it done. â€¢ Testing partner for haemoglobinopathy. The risk of SCD in offspring is 50 % if the biologic father is heterozygous; the risk is 100 % if he is homozygous. B. Medications During Pregnancy 1. Folic acid supplementation (0.4-0.8 mg/day) is recommended for all women of reproductive age to reduce the risk of neural tube defects in offspring. There is consensus opinion among experts that the dose should be higher in women with SCD to accommodate this requirement, as well as routine pregnancy requirements and SCD requirements related to haemolysis. A dose of 5 mg/day has been recommended as likely to satisfy all of these needs. 2. Hydroxyura: Many patients will be on hydroxyurea therapy. Exposure to hydroxyurea, alone or in combination with other drugs, has been reported in fewer than 100 human pregnancies, including approximately 40 first trimester exposures [2]. An increase in major congenital defects was not observed in these limited human data, but has been reported in animal studies. Given the relatively small number of exposed pregnancies and the observation that hydroxyurea produced malformations in animal studies, it is prudent to discontinue hydroxyurea three months before conception [3] 3. Iron chelator: Women on iron chelation therapy may continue this therapy until they conceive, but it should be discontinued at that time. In experimental animal studies, deferasirox did not increase the risk of congenital anomalies at doses lower than those used in humans, but deferoxamine was associated with congenital anomalies in some animal studies. Data from exposure in humans are limited especially for deferasirox, but no toxic or teratogenic effects have been reported. Both drugs are FDA pregnancy category C. Deferiprone is pregnancy category D. Untreated women with excessive iron stores should consider delaying pregnancy until treatment has

been completed. 4. Prophylactic penicillin: Prophylactic penicillin therapy may be continued during pregnancy. Penicillin has an excellent maternal-fetal safety profile for use in pregnancy. We do not routinely initiate penicillin prophylaxis because of pregnancy but continue it in patients who are already taking prophylaxis. 5. Analgesia: Pain can be managed using standard therapies. However, non-steroidal anti-inflammatory drugs (NSAIDs) may interfere with ovulation, thereby reducing the probability of conception. Whether NSAID use in the first trimester increases the risk of miscarriage or cardiac defects is unclear; epidemiologic studies have reported conflicting results. NSAIDs are generally avoided after 30 weeks of gestation because of the risk of premature narrowing or closure of the ductus arteriosus C. Pregnancy Outcomes in SCD: There is consistent evidence that anemia and vasoocclusive or painful crises occur more often in pregnancy and are the most common maternal SCD complications associated with pregnancy, occurring in over 50 % of pregnant women with SCD [4]. Painful crises are more common with advancing pregnancy and postpartum. The largest data set of SCD outcomes in pregnant women is the Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project of the US Agency for Healthcare Research and Quality, which analyzed all pregnancy-related discharges with a diagnosis of SCD for the years 2000-2003, and included almost 18,000 deliveries to women with SCD and 17 million deliveries to women without the disease [5] Compared with women without SCD, women with SCD were at increased risk of: â€¢ Maternal death-While women with SCD accounted for 0.1 % of the pregnancies, they accounted for 1 % of all maternal deaths. There were 10 deaths in the SCD group (mortality 72 deaths per 100,000 deliveries versus 12.7 deaths per 100,000 deliveries in women without SCD). â€¢ Transfusion â€¢ Systemic Inflammatory Response Syndrome. â€¢ Pneumonia. â€¢ Sepsis. â€¢ Asymptomatic bacteriuria. â€¢ Cerebral vein thrombosis. â€¢ Deep vein thrombosis. â€¢ Genitourinary tract infection. There was no statistical difference in rates of stroke, pyelonephritis, pulmonary embolus, or myocardial infarction. Pregnancy outcome: The Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project described above also reported pregnancy outcomes [5]. Compared with pregnant women without SCD, women with SCD were at increased risk of: â€¢ Intrauterine growth restriction (IUGR) â€¢ Eclampsia â€¢ Gestational hypertension and preeclampsia â€¢ Preterm labour â€¢ Postpartum infection â€¢ Abruption â€¢ Antepartum bleeding Normal delivery of Caesarean section? Medical and obstetrical complications would be expected to result in an increased risk of preterm birth less than 37 weeks. The caesarean delivery rate tends to be higher in women with SCD. The increased rate is related to a higher frequency of pregnancy complications, and some centers have policies for short trials of labour and early operative intervention at the first sign of a nonreassuring foetal heart rate tracing. Summary: Special precaution and counselling should be offered to all pregnant females with SCD. Adequate training should be given to medical and paramedical staff at rural hospitals. Clear guidelines should be framed with regards to the medications and the management of complications in such pregnancies.

88. HB D-Punjab: A single centre largest experience on HPLC from Punjab

2020

Indian Journal of Hematology and Blood Transfusion

Narang, V and Jain, A and Garg, B and Sood, N

Aims & Objectives: To analyze the clinical, hematological and chromatographic parameters of patients with HbDPunjab syndromes. Patients/Materials & Methods: A total of 3139 blood samples (both pediatric and adult) were screened for hemoglobinopathies and structural hemoglobin variants by using Bio-Rad D10 variant for evaluation of anemia and for family and antenatal screening studies. The clinical, hematological, and chromatographic parameters of individual HbDPunjab syndromes comprising of heterozygous (HbA/ D) and compound heterozygous states Î²-thalassemia trait (HbD/Î²) were correlated and analyzed. Results: A total of 405 cases of structural hemoglobin variants comprising of Î² thalassemia, HbS, HbE, HbD-Punjab, HbD Iran, HbQ India and HbJ-Meerut were detected. HbDP syndromes constituted 42 cases (10.3%) of all hemoglobin variants and 1.34% of all the samples screened for hemoglobinopathies. Heterozygous HbDP constituted 38 of 42 (90.5%) cases and Compound heterozygous for HbD Punjab and beta thalassemia constituted 04 of 42 cases (9.5%). HbD was detected among both young and old individuals with an age range of 1-54 years. Clinically significant pallor was noted in HbA/D and HbD/Î² groups. Icterus was present in one case both in HbA/D and HbD/Î². Splenomegaly was seen in two of four HbD/Î² patients. Three cases of HbA/D and one case of HbD/Î² required blood transfusion.

Discussion & Conclusion: HbDP is not an uncommon hemoglobinopathy in India. Heterozygous state is a clinically asymptomatic state. CE-HPLC has the advantage of rapid detection and accurate quantitation.

89. Hb SE disease: A clinico-hematological profile

2005

Annals of Hematology

Mishra, P and Pati, H P and Chatterjee, T and Dixit, A and Choudhary, D R and Srinivas, M U and Mahapatra, M and Choudhry, V P

Hb S and Hb E are globally common hemoglobinopathies. However, Hb SE double heterozygous state is uncommon, with only 25 cases reported so far in literature. We present two more cases. One presented with gallstones, and the other was asymptomatic. This type of disorder was previously described as a relatively asymptomatic condition compared to HbSS. A review of the 25 reported cases in literature shows that 40.7% (11/27) of these cases are symptomatic. Gender, hematological parameters and levels of Hb S, E or F do not predict clinical severity. Â© Springer-Verlag 2005.

90. Biochemical characterisation of spectrum of hemoglobinopathies and thalassemia syndromes - experience with 689 cases in a tertiary care hospital in South India

2013

International Journal of Pharma and Bio Sciences

Chandran, P and Laxmi, M S and Yadagiri, B and Noorjahan, M and Nageshwar Rao, M

The inherited diseases of hemoglobin have remarkable phenotypic variability because of genetic modifiers necessitating medical intervention at various stages of disease. Genotype-phenotype relationship is crucial in this regard. So three year retrospective study of biochemical pattern of Hemoglobinopathies and Thalassemias and their clinical manifestations was done in a cohort of 689 patients in a tertiary care hospital. The highest incidence was Sickle cell disease (15.8%) followed by Sickle cell trait (13.1%), Thalassemia minor (11.8%), HbS/Î²-thalassemia (5.7%), Thalassemia major (1.6%). Less frequent were HbH disease, HPFH, Thalassemia intermedia, HbE, HbS/HbD, HbE/Î²-thalassemia, HbS/HPFH, HbD/Î²-thalassemia, HPFH/Î²-thalassemia, Î´Î² trait and HbQ. Males had significantly higher incidence (55.2%). Thalassemia major had reduced HbA2 (1.9%). HbAS/Î±-thalassemia had higher mean age and low HbS as compared to Sickle cell trait. HbS/Î²0-thalassemia had lower mean age and higher HbA2, HbS than HbS/Î²+-thalassemia, corresponding with severity of disease. To conclude biochemical characterisation closely correlates with the clinical phenotype enabling correct diagnosis and avoids unnecessary investigations.

91. Sickle cell disease associated arrhythmias and inâ€hospital outcomes: Insights from the National Inpatient Sample

2020

Journal of Arrhythmia

***Patel, Upenkumar and Desai, Rupak and Hanna, Bishoy and Patel, Dhruval and Akbar, Shahzad and Zubair, Mohammed and Kumar, Gautam and Sachdeva, Rajes*h**

BackgroundThe frequency and temporal trend in the prevalence of arrhythmias and associated inâ€hospital outcomes in patients with sickle cell disease (SCD) have never been quantified.MethodsOur study cohort of SCD patients and subâ€types of arrhythmias were derived from the 2010â€2014 National Inpatient Sample using relevant diagnostic codes. The frequency and trends of arrhythmia and odds of inpatient mortality were measured.Results A total of 891Â 450 hospitalized SCD patients were identified, of which, 55Â 616 (6.2%) patients experienced arrhythmias. The SCD cohort with arrhythmia demonstrated higher allâ€cause mortality (2.7% vs 0.4%; adjusted OR 2.53, 95% CI 2.15â€2.97, PÂ <Â .001), prolonged hospital stays (6.9 vs 5.0Â days)

and higher hospital charges ($53Â 871 vs $30Â 905) relative to those without arrhythmias (PÂ <Â .001).The frequency of supraventricular arrhythmia (AFib, SVT, and AF) and ventricular arrhythmia (VFib and VT) were 1893 and 362 per 100Â 000 SCDâ€relatedadmissions, respectively. Unspecified arrhythmias (4126) were seen most frequently followed by AFib (1622) per 100Â 000 SCDâ€relatedadmissions. From 2010 to 2014, the frequency of any arrhythmias and atrial fibrillation in hospitalized SCD patients relatively increased by 29.6% and 38.5%, respectively. There was nearly a twofold (2.4% in 2010 to 5.0% in 2014) increase in the frequency of arrhythmia among patients aged <18Â years. The frequency of arrhythmias in hospitalized male and female SCD patients relatively increased by 28.8% and 31.4%, respectively (PtrendÂ <Â .001).ConclusionsThe frequency of arrhythmias among SCD patients is on the rise with worse hospitalization outcomes, including higher inâ€hospital mortality and higher resource utilization as compared to those without arrhythmias.

92. Epidemiological Study of Glucose-6-phosphate Dehydrogenase Deficiency in Scheduled Caste Population of India

2012

Journal of Anthropology

Rai, Vandana and Kumar, Pradeep

The aim of the present study was to determine the glucose-6-phostphate dehydrogenase (G6PD) deficiency in scheduled caste (SC) population of eastern Uttar Pradesh, India. After taking clearance certificate from the Institutional Ethics Committee, blood samples were collected from total 200 healthy individuals belonging to scheduled caste. G6PD deficiency analysis was done by methemoglobin test according to the method of Brewer et al. (1962). Out of 200 samples, 20 individuals were glucose-6-phosphate dehydrogenase deficient and 22 samples were heterozygous that is, carriers. The percentage of G6PD deficient (Gd+/+) and G6PD carrier (Gd+/Gd-) phenotypes were 10% and 11%, respectively. The frequency of mutant allele (Gd-) was observed 0.172. Early detection and prevention is the key strategy for successful management and control of this genetic disease. [PUBLICATION ABSTRACT]

93. Genetic Disorders in Haematological Practice in India

2002

Community Genetics

Mohanty, D and Colah, R B and Gorakshakar, A C and Nadkarni, A H and Phanasgaonkar, S P and Shetty, S and Ghosh, K and Mukherjee, M B

Symposium on Community Genetics in Developing Countries. January 16-18, 2002, Bangalore, India. Guest Editor: Alan H. Bittles, Perth Haemoglobinopathies represent a significant national health burden in India. The distribution of specific disorders varies geographically and by community. Heterozygote frequencies of [beta]-thalassaemia range from 1 to 15%, resulting in an estimated 20 million carriers. HbS is mainly present in tribal and non-caste communities, with carrier prevalences of up to 40%. By comparison, [alpha]-thalassaemia carriers are found in both the caste and tribal communities, and can reach a frequency of >90% in the latter case. Community control of haemoglobinopathies relies mainly on out-reach education programmes and genetic counselling, with antenatal diagnosis offered in specific major centres. Only partial data are available on the prevalence of haemophilia, but it has been estimated that there are some 50,000 affected individuals nationwide, with an additional 1,500 new cases born each year. RFLP-based techniques have been established to detect mutations in the factor VIII and IX genes, enabling the limited introduction of carrier detection and antenatal diagnosis.

94. Comparison of in-vitro and in-vivo response to fetal hemoglobin production and [gamma]-mRNA expression by hydroxyurea in Hemoglobinopathies

2013

Indian Journal of Human Genetics

Italia, Khushnooma and Jijina, Farah and Merchant, Rashid and Swaminathan, Suchitra and Nadkarni, Anita and Gupta, Maya and Ghosh, Kanjaksha and Colah, Roshan

Background: Hydroxyurea, which induces Fetal hemoglobin (HbF) synthesis, is the only drug widely used in different hemoglobinopathies; however, the response is very variable. We compared the efficacy of hydroxyurea in-vitro in erythroid cultures and in-vivo in the same patients with different hemoglobinopathies to induce HbF production and enhance Î³-messenger RNA expression. Materials and Methods: A total of 24-patients with different Hemoglobinopathies were given hydroxyurea and their response was studied in-vivo and in-vitro on mononuclear cells collected from them simultaneously. Results: A total of 57.7% of patients (responders) showed no further crisis or transfusion requirements after hydroxyurea therapy with a mean increase in fetal cells (F-cells) of 63.8 +- 59.1% and Î³-mRNA expression of 205.5 +- 120.8%. In-vitro results also showed a mean increase in F-cells of 27.2 +- 24.7% and Î³-mRNA expression of 119.6% +- 65.4% among the treated cells. Nearly 19.0% of the partial-responders reduced their transfusion requirements by 50% with a mean increase in F-cells of 61.2 +- 25.0% and 28.4 +- 25.3% and Î³-mRNA-expression of 21.0% +- 1.4% and 80.0% +- 14.1% in-vivo and in-vitro respectively. The non-responders (15.3%) showed no change in their clinical status and there was no significant increase in F-cells levels and Î³-mRNA expression in-vivo or in-vitro. Conclusion: Thus, this method may help to predict the in-vivo response to hydroxyurea therapy; however, a much larger study is required.

95. Physical growth of children with sickle cell disease

2004

Indian Journal of Human Genetics

Mukherjee, Malay and Gangakhedkar, R

Anthropometric measurements were used to study the physical growth of 58 sickle cell disease(SS) children with severe clinical manifestations and compared with 86 normal(AA) children from Nagpur district of Maharashtra. Both sickle cell disease male and female children were shown to have statistically significant lower weights, heights, sitting heights, mid arm circumferences, skin fold thickness and body mass indexes but not upper/ lower segment ratio as compared to normal children with comparable sex and ages. No significant differences were observed between the male and female children with sickle cell disease or normal for any of the anthropometric measurements. A significant lower values of all the measurements except U/L ratio was observed in the age group of 11-14 years than the earlier age among the sickle cell disease children as compared to the normal children of the same age and sex groups. Thus, these results indicate that as a group, children with sickle cell disease weigh less, are shorter and undernourished as compared to normal children.

96. The case for dedicated sickle cell centres

2006

Indian Journal of Human Genetics

Serjeant, Graham

Serjeant comments on the need for dedicated Sickle Cell Centers in India. Sickle cell disease is an inherited blood condition resulting from the inheritance of abnormal genes from both parents. In India, the sickle cell gene has been reported in 73% of studies among tribal people, 17% among lower castes, 9% among middle castes and 1%

among higher castes. Whether the disease occurs in India, Africa, south or north America, the Caribbean or Europe, a case could be made for delivery of health care through dedicated Sickle Cell Centers.

97. Status of Antioxidants Vitamin and Plasma Malondialdehyde (MDA) in Sickle Cell Anaemia Patients of Chhattisgarh Region

2014

International Journal of Contemporary Medicine

Gupta, Vikas Kumar and Singh, Neelima and Nigam, Prashant and Shah, Jayant and Patil, S K B

Sickle cell spontaneously generates approximately two times more amount of reactive oxygen species. Lipid per oxidation has a major role in the pathophysiology of sickle cell anaemia, this may overwhelm the antioxidant defence system. Therefore, the study was undertaken to evaluate the levels of plasma Malondialdehyde (MDA), and antioxidants vitamins. The present study was carried out in the Department of Biochemistry, Chhattisgarh Institute of Medical Sciences, Bilaspur, Chhattisgarh. Total eighty subjects were age between 15-35 years both male and female was selected for this study. We found significantly (P<0.001) elevated plasma MDA level and the antioxidants vitamins level were reduced significantly (P<0.001) in homozygous sickle cell cases as compared to controls. These observations provide the evidence of imbalance between oxidant and antioxidant status leading to chronic oxidative stress. Therefore supplementation with antioxidants vitamin may ameliorate some of the sickle cell symptoms and improve quality of life.

98. Relationship between somatic problems and their coping strategies among sickle cell anaemic adolescents

2016

Indian Journal of Health and Wellbeing

Ogre, Shyama C and Chakravarty, Moyna and Shrivastava, Priyamvada and Janghel, Gaukaran

Out of total sample of the study 72.7 % adolescents were homozygous and 76.7 % were heterozygous. Male and females of Age group 14-16 years were maximum number. Percentage of heterozygous males complaining somatic problems is higher, whereas percentage of homozygous females complaining somatic problems is high. There is significant positive relationship between Maladaptive coping style and somatic problems. Somatic problems emerge as significant predictor in variation of criterion variable somatic problems. The t values explain significant difference in somatic complaints among sickle cell adolescents with respect to gender and zygosity.

99. Prevalence of Hemoglobinopathies in Tribal Region of India: A Retrospective Observational Study

2020

Advances in Biosciences & Clinical Medicine

Dulhani, Naveen and Koshewara, Pratima and Bharti, Rupendra K and Sharma, Sanat K

Hemoglobinopathies are the common inherited diseases around the world. Thalassemia & sickle cell disease are the important challenges for tribal populations in India. Many study demonstrated the prevalence of haemoglobinopathies in India & among tribes of India but limited data available from Baster tribal region. This study will further lightens the haemoglobinopathies among Baster region of Chhattisgarh state of India. Methods: It was an retrospective observational study, carried out in Late. BRKM Government Medical College, Dimrapal, Jagdalpur which was located at baster region of Chhattisgarh state of India aims to determine the prevalence of various hemoglobinopathies in Baster. Out of 421 suspected patientâ€™s screened for hemoglobinopathies by Capillary electrophoresis. Statistical Package for Social Sciences (SPSS) used for descriptive analysis. Results: Out of 421 cases, 276 were diagnosed with various type of hemoglobinopathies {49% has HbAS (sickle cell

anaemia trait), 3% HbSS (sickle cell disease), 6% sickled beta-thalassemia & 8% HPFH (hereditary persistence of foetal hemoglobin)}. Non-tribal population has higher trends of sickled beta thalassemia 14 (8.28%), Hereditary persistence of foetal hemoglobin 26 (15.38%) and HbAS 122 (72.19%) as compare to tribal population but there was similar prevalence of HbSS among both of these groups. Conclusion: In India, hemoglobin disorders are the great threat for tribal population. As <10% of tribes residing in India and many were extinct. The non-tribal community has more prevent than tribal communities.

100. Hematological profile of pregnant women with carrier status of hemoglobin disorders in Coastal Odisha, India

2011

International Journal of Child Health and Human Development

Balgir MSc Hons, PhD, Ranbir S

Hemoglobin disorders are commonly encountered maladies throughout the Indian subcontinent. Pregnant women constitute an important segment of the society. Genetic screening in pregnant women is mandatory for the detection of hemoglobin disorder in the absence of any response to diet therapy. This cross sectional study was undertaken to assess the hemato-physiological stress during different trimesters and to identify hemoglobinopathies following the standard methodology and techniques in 178 pregnant women of Coastal Odisha in Central Eastern region of India. An incidence of 13.5% hemoglobinopathies was recorded in pregnant women which was alarmingly high in the coastal state of Odisha. Statistically significant reduced profile of mean hematological indices was observed in pregnant women with carrier hemoglobin disorders against the matched normal controls. A consistent significant decrease in the mean red cell indices was noted in 1st and 2nd trimesters of pregnant women with sickle cell trait and Î²-thalassemia carrier as against the matched normal pregnant women. However, significant improvement with the nutritional supplementations and prophylactic measures in the 3rd trimester have shown almost similar hematological indices of pregnant women with Î²-thalassemia trait, hemoglobin AE, and sickle cell trait, to those of matched normal pregnant women. It is concluded that genetic screening for the detection of hemoglobin disorders in pregnant woman is highly essential for the regular check up, antenatal care, **and clinical management right from the conception to delivery in India.**

101. Epidemiology & social costs of haemophilia in India

2014

The Indian Journal of Medical Research

Kar, Anita and Phadnis, Supriya and Dharmarajan, Sumedha and Nakade, Juhi

India lacks a national policy on the prevention and control of genetic disorders. Although the haemoglobinopathies have received some attention, there are scarce data on the epidemiology of other genetic disorders in India. Haemophilia, an inherited single gene disorder with an incidence of 1 per 10,000 births, manifests as spontaneous or trauma-induced haemorrhagic episodes in patients, progressing to chronic disability and premature mortality in untreated patients or patients with sub-optimal treatment. Although the genetic basis of this disorder has been well studied in India, data on the number of patients, trends of the disorder in India, social costs of the condition and opportunities and competencies for offering genetic counselling through a public health programme have not been reported. This review article summarizes the available Indian data, which show that the country harbours the second highest number of global patients with haemophilia A. The reported number of patients with haemophilia A is 11,586 while the estimated prevalence could be around 50,000 patients. This review also identifies the need to immediately initiate a national programme for haemophilia, with components of prevention, care for patients, surveillance and education and support for families.

102. Seroepidemiology of parvovirus B19 among different age groups & pregnant women in India

2017

The Indian Journal of Medical Research

Viswanathan, Rajlakshmi and Tandale, Babasaheb and Tamayachekar, Manisha and Jadhav, Santoshkumar and Khutwad, Kirtee and Munne, Kiran

B19 infection can lead to serious consequences in â€˜at riskâ€™ groups, such as organ transplant recipients, thalassaemia and sickle cell anaemia patients and foetus in utero[6]. Anonymized, archived serum samples collected from hospital staff, general practitioners, school children and staff who were surveyed as the risk group for pandemic flu infection in Pune district, in 2009[10], were tested for estimating community seroprevalence. [...]our study provided baseline data from India, on seroprevalence of B19 in healthy pregnant women.

103. Orofacial manifestations of hematological disorders: Anemia and hemostatic disorders: Official Publication of Indian Society for Dental Research

2011

Indian Journal of Dental Research

Adeyemo, Titilope and Adeyemo, Wasiu and Adediran, Adewumi and Akinbami, Abd Jaleel and Akanmu, Alani

The aim of this paper is to review the literature and identify orofacial manifestations of hematological diseases, with particular reference to anemias and disorders of hemostasis. A computerized literature search using MEDLINE was conducted for published articles on orofacial manifestations of hematological diseases, with emphasis on anemia. Mesh phrases used in the search were: oral diseases AND anaemia; orofacial diseases AND anaemia; orofacial lesions AND anaemia; orofacial manifestations AND disorders of haemostasis. The Boolean operator "AND" was used to combine and narrow the searches. Anemic disorders associated with orofacial signs and symptoms include iron deficiency anemia, Plummer-Vinson syndrome, megaloblastic anemia, sickle cell anemia, thalassaemia and aplastic anemia. The manifestations include conjunctiva and facial pallor, atrophic glossitis, angular stomatitis, dysphagia, magenta tongue, midfacial overgrowth, osteoclerosis, osteomyelitis and paraesthesia/anesthesia of the mental nerve. Orofacial petechiae, conjunctivae hemorrhage, nose-bleeding, spontaneous and post-traumatic gingival hemorrhage and prolonged post-extraction bleeding are common orofacial manifestations of inherited hemostatic disorders such as von Willebrand's disease and hemophilia. A wide array of anemic and hemostatic disorders encountered in internal medicine has manifestations in the oral cavity and the facial region. Most of these manifestations are non-specific, but should alert the hematologist and the dental surgeon to the possibilities of a concurrent disease of hemopoiesis or hemostasis or a latent one that may subsequently manifest itself.

104. Gene frequency of sickle cell trait among Muslim populations in a malarial belt of India, i.e., Manipur

2012

The Egyptian Journal of Medical Human Genetics

Shah, Ahsana and Hussain, Ruqaiya and Fareed, Mohd and Afzal, Mohammad

105. Oxidative stress in diabetic patients with sickle-cell anemia: A warning call for endemic areas

2018

International Journal of Applied and Basic Medical Research

Mahajan, Rajiv

It has been reported that the oxidative stress is a major outcome of diabetes mellitus (DM) affecting red cell antioxidant enzymes, and this in turn can lead to reduced hemoglobin concentrations in diabetic patients. A comparative study conducted on healthy individuals (CONT), individuals with type 2 DM (T2DM) or SCT, and patients with both T2DM and SCT (T2DM-SCT), comparing vascular function, hemorheological profile, and biomarkers of oxidative stress, inflammation, and nitric oxide metabolism found that oxidative stress, advanced glycation end products, and inflammation (interleukin-1 Î²) were greater in patients with T2DM-SCT compared with the other groups. In another study, normoglycemic patients with SCD demonstrated impaired Î²-cell function with reduced insulin secretion even before oral glucose tolerance test was impaired.

106. Skeletal scintigraphy manifestations of hematologic disorders

2012

Indian Journal of Nuclear Medicine : IJNM

Solav, Shrikant and Bhandari, Ritu and Solav, Pallavi

Skeletal manifestations are common in hematologic disorders. Benign entities such as Sickle cell disease develop microvascular embolization causing skeletal crisis. Leukemia, acute myeloblastic or lymphoblastic may develop bone marrow infarcts. Compromised immunity makes them susceptible to secondary infection leading to osteomyelitis or septic arthritis. Exposure to steroids may lead to osteonecrosis in these cases. Presented here is an atlas of various scintigraphic skeletal manifestations encountered over the past 10 years, in hematologic disorders.

107. Alpha thalassaemia in tribal communities of coastal Maharashtra, India

2014

The Indian Journal of Medical Research

Deo, Madhav and Pawar, Prakash

Background & objectives: In a routine community health survey conducted in adult Adivasis of the costal Maharashtra, microcytosis and hyprochromia were observed in more than 80 per cent of both males and females having normal haemoglobin levels suggesting the possibility of Î±-thalassaemia in these communities. We conducted a study in Adivasi students in the same region to find out the magnitude of Î±-thalessaemia. Methods: The participants (28 girls and 23 boys) were 14-17 yr old studying in a tribal school. Fasting venous blood samples (5 ml) were subjected to complete blood count (CBC), Hb-HPLC and DNA analysis using gap-PCR for deletion of - Î±3.7 and - Î±4.2, the two most common molecular lesions observed in Î±-thalassaemia in India. Results: Microcytic hypochromic anaemia was observed 50 and 35 per cent girls and boys, respectively. Iron supplementation improved Hb levels but did not correct microcytois and hypochromia. m0 ore than 80 per cent non-anaemic students of both sexes showed microcytois and hypochromia. DNA analysis confirmed that the haematological alterations were due to Î±-thalassaemia trait characterized by deletion of - Î±3.7. Majority (> 60%) of the affected students had two deletions (-Î±3.7/-Î±3.7 genotype Î±+ thalassaemia. Interpretation & conclusions: This is perhaps the first report on the occurrence of Î±-thalassaemia in tribal communities of coastal Maharashtra. Very high (78.4%) haplotype frequency of -Î±3.7 suggests that the condition is almost genetically fixed. These preliminary observations should stimulate well planned large scale epidemiological studies on Î±-thalassaemia in the region.

108. Frequency of [beta]-thalassemia trait and other hemoglobinopathies in northern and western India

2010

Indian Journal of Human Genetics

Madan, Nishi and Sharma, Satendra and Sood, S and Colah, Roshan and Bhatia, H

Introduction : India is an ethnically diverse country with an approximate population of 1.2 billion. The frequency of beta-thalassemia trait (Î²TT) has variously been reported from < 1% to 17% and an average of 3.3%. Most of these studies have been carried out on small population groups and some have been based on hospital-based patients. There is also a variation in the prevalence of hemoglobinopathies in different regions and population groups in the country. A high frequency of Hb D has been reported from the North in the Punjabi population, Hb E in the eastern region of India and Hb S is mainly reported from populations of tribal origin from different parts of the country. Objectives: To study the gene frequency of Î²TT and other hemoglobinopathies in three regions East (Kolkata), West (Mumbai) and North (Delhi) in larghe population group (schoolchildren) for a more accurate assessment of gene frequency for planning of control programmes for haemoglobinopathies. Materials and Methods: This study included 5408 children from 11 schools in Delhi, 5682 from 75 schools in Mumbai and 957 schoolchildren from Kolkata who were screened for Î²TT and haemoglobinopathies. These included 5684 children from 75 schools in Mumbai and 5408 children from 11 schools in Delhi. Children were 11-18 years of age of both sexes. The final report is, however, only on 11090 schoolchildren from Mumbai and Delhi as data from Kolkata was restricted both in numbers and objectives and could not be included for comparison. Results: The overall gene frequency of Î²TT in Mumbai and Delhi was 4.05% being 2.68% and 5.47% in children of the two cities respectively. In Mumbai, the gene frequency was evenly distributed. Majority of the children with Î²TT from Mumbai were from Marathi (38.9%) and Gujarati (25%) speaking groups. Gene frequency was >5% in Bhatias, Khatris, Lohanas and Schedule Castes. In Delhi, a higher incidence was observed in schoolchildren of North and West Delhi (5.8-9.2%). The schoolchildren of North and West Delhi comprised predominantly of Punjabi origin compared to children in the South of the city (2.2%, 2.3%). When analyzed state-wise, the highest incidence was observed in children of Punjabi origin (7.6%) and was >4% from several other states. Majority of the traits from Mumbai were anemic (95.1% male and 85.6% in female). The prevalence of anemia was lower (62.7% male and 58.4% female) children with Î²TT from Delhi. This was a reflection of the higher prevalence of anemia in children without hemoglobinopathy in Mumbai than in Delhi. Nutritional deficiency was probably more severe and rampant in children Mumbai. Gene frequency of Hb D was greater in schoolchildren from Delhi (1.1%) than in Mumbai (0.7%). Hb S trait (0.2%) was observed exclusively in children from Mumbai. A low incidence of Hb E trait (0.04%) was seen in children in Mumbai. A higher incidence is reported from the East. The number of cases studied from the eastern region was small as the data from the East (Kolkata) could not be included in the analysis. Conclusion: This study comprises a larger number of children studied for the gene frequency of Î²TT and other hemoglobinopathies from India. Population groups with higher gene frequencies require screening programmes and facilities for antenatal diagnosis as well as increased awareness and educational programmes to control the birth of thalassemic homozygotes. The overall carrier frequency of Î²TT was 4.05% and reinforces the differential frequency of Î²-thalassemia trait in schoolchildren from Delhi and Mumbai and the higher incidence of hemoglobin D in Punjabis as reported previously. The birth incidence calculated thereof for homozygous thalassemics would be 11,316 per year which are added each year to the existing load of homozygous thalassemics. This is much higher than the previously reported number of births annually. Hence suitable control measures need to be undertaken urgently in India.

109. Number of Children With Sickle Cell Anemia Increasing Worldwide: The Journal of the American Medical Association

2013

JAMA

Friedrich, M J

The number of children born with sickle cell anemia is increasing around the world, with the majority in sub-Saharan Africa and India and the number of newborns with the condition could reach almost half a million by 2050, according to a report from an international group of researchers. By combining epidemiologic estimates of the frequency of sickle cell anemia and projected birth rates of those with the disease, the researchers calculated the number of newborns with sickle cell anemia for each five-year interval between 2010 and 2050.

110. Characterisation of anaemia and associated factors among infants and pre-schoolers from rural India

2016

Public Health Nutrition

Nair, Krishnapillai Madhavan and Fernandez-Rao, Sylvia and Nagalla, Balakrishna and Kankipati, Radhakrishna Vijaya and Punjal, Ravinder and Augustine, Little Flower and Hurley, Kristen M and Tilton, Nicholas and Harding, Kimberly B and Reinhart, Greg and Black, Maureen M

Objective In India, national databases indicate anaemia prevalence of 80 % among 6-35-month-old children and 58 % among 36-59-month-old children. The present study aimed to characterise anaemia and the associated factors among infants and pre-schoolers living in rural India. Design Multivariate logistic regression analysis of data collected prior to an intervention trial. Fe-deficiency with anaemia (IDA), Fe deficiency with no anaemia (IDNA) and anaemia without Fe deficiency were defined. Serum ferritin, soluble transferrin receptor (sTfR) and sTfR/log ferritin index were used to indicate Fe status. Setting Twenty-six villages of Nalgonda district, Telangana, India. Data were collected in community sites. Participants Four hundred and seventy-six infants (aged 6-12 months), 316 pre-schoolers (aged 29-56 months) and their mothers. Results Prevalence of anaemia among infants and pre-schoolers was 66Â·4 and 47Â·8 %, prevalence of IDA was 52Â·2 and 42Â·1 %, prevalence of IDNA was 22Â·2 and 29Â·8 %, prevalence of anaemia without Fe deficiency was 14Â·2 and 5Â·7 %. Among infants, anaemia was positively associated with maternal anaemia (OR=3Â·31; 95 % CI 2Â·10, 5Â·23; P<0Â·001), and sTfR/log ferritin index (OR=2Â·21; 95 % CI 1Â·39, 3Â·54; P=0Â·001). Among pre-schoolers, anaemia was positively associated with maternal anaemia (OR=3Â·77; 95 % CI 1Â·94, 7Â·30; P<0Â·001), sTfR/log ferritin index (OR=5Â·29; 95 % CI 2Â·67, 10Â·50; P<0Â·001), high C-reactive protein (OR=4Â·39; 95 % CI 1Â·91, 10Â·06, P<0Â·001) and young age (29-35 months: OR=1Â·92; 05 % CI 1Â·18, 3Â·13, P=0Â·009). Conclusions Anaemia prevalence continues to be high among infants and pre-schoolers in rural India. Based on sTfR/ferritin index, Fe deficiency is a major factor associated with anaemia. Anaemia is also associated with inflammation among pre-schoolers and with maternal anaemia among infants and pre-schoolers, illustrating the importance of understanding the aetiology of anaemia in designing effective control strategies.

111. Significance of Mentzer Index and Erythrocyte Indices to Evaluate Erythrocyte Morphology and Spectrum of Anemia in Adult Population in a Tertiary Care Hospital in Rural Haryana

2020

JK Science

Sharma, Abhimanyu and Lone, Aasif Hamid and Sharma, Mehak and Chaudhry, Manish

Anemia, reduced red cell mass below normal range, results in reduction of oxygen carrying capacity of blood that results in tissue hypoxia. MCV, MCH, MCH and RDW represent a sensitive indicator to study erythrocyte morphology. Mentzer Index recommended MI<13 to be suggestive of Ã¢-TT and MI>13 for Iron deficiency anemia. 100 cases were analyzed prospectively over a span of 1 year at MMIMSR, Mullana. The study revealed 34% of patients to be in age group of 21-30 years with (59%) female predominance out of which majority of cases were of moderate anemia (73%). Erythrocyte indices revealed pattern with majority of samples having MCV, MCH and MCHC to be in normal range while RDW showed increased values. Mentzer index came out to be >14 in 96% of samples. To conclude evaluation of erythrocyte indices and Mentzer index aids in quatitative assessment of anemia and also to distinguish between iron deficiency anemia and thalassemia trait.

112. Care-Related Quality of Life of Caregivers of Beta-Thalassemia Major Children: An Epidemiological Study in Eastern India

2020

Journal of Epidemiology and Global Health

Biswas, Bijit and Naskar, Narendra Nath and Basu, Keya and Dasgupta, Aparajita and Basu, Rivu and Paul, Bobby

Caregivers are the persons who provide care at the time of distress or illness. They face many stress and strain to provide the best possible medical care for their children. There are very few studies that explored the care-related quality of life (CarerQoL) of the caregivers of thalassemic children and its correlates. With this background, the current study was designed to explore the CarerQoL of the caregivers of Î²-Thalassemia Major (Î²-TM) children and its various correlates. It was a cross-sectional observational study conducted among caregivers of Î²-TM children attending a tertiary care health facility of Eastern India in between May 2016 and April 2017 with a structured schedule. The median CarerQoL score was found to be 5 with an interquartile range of 4â€“7 (range: 11). In the final multivariable logistic regression model, care receiversâ€™ (thalassemic children) age [adjusted odds ratio (AOR): 2.2 (1.2â€“4.2)], spleen status [AOR: 4.1 (2.0â€“8.7)], blood transfusion frequency [AOR: 2.1 (1.1â€“3.9)], and quality of life (QoL) [AOR: 3.0 (1.6â€“5.5)] and caregiversâ€™ educational level [AOR: 2.3 (1.2â€“4.1)], perceived social discrimination [AOR: 2.3 (1.3â€“4.1)], debt [AOR: 2.3 (1.2â€“4.3)], nongovernmental organization assistance [AOR: 2.0 (1.0â€“4.0)], and wage loss due to seeking treatment [AOR: 1.9 (1.1â€“3.4)] were significant predictors of CarerQoL of the study participants adjusted with their age, sex, working status, per-capita monthly income, knowledge level related to the disease, and care receiversâ€™ comorbidity status. To conclude, CarerQoL of the study participants were significantly associated with QoL of their wards. Other significant associates of CarerQoL were caregiversâ€™ education level, financial profile, patientsâ€™ age, and their clinico-therapeutic profile.

113. Genetic heterogeneity and population structure of Gond-related tribes in the Vidarbha region of Maharashtra

1992

Human Biology

Rao, V R and Sathe, M S and Gorakshakar, A C and Vasantha, K

Genetic heterogeneity in nine polymorphic loci is observed among Gond-related tribes in the Vidarbha region of Maharashtra. Pardhans, with their high ABO*A2 gene frequency (4.01%), low m gene frequency (57%), high P*1 gene frequency (42.7%), and high HbS trait (31.58%), differ significantly from other tribes. Per locus average heterozygosity among the studied tribes ranged from 36.24% to 40.37%, with Pardhans being more heterozygous. Analysis by FST and the empirical relationship between average allele frequencies and the ratio of within-gene to total gene diversity show that the tribes are isolated and that differentiation among them is at an early stage and approximately in conformity with expected differentiation under genetic drift. However, distances and principal components analysis reveal that Pardhans are far removed from the other tribes and from other central Dravidian tribes. Furthermore, of the various demographic parameters estimated, the high average heterozygosity in Pardhans is significantly correlated with mean marital distance (MMD), regression of MMD on wife's age, and effective population size. There is congruence between genetic and demographic data, showing that Pardhans are distinct. This conforms with Haimendorf's (1979) contention based on cultural traits that Pardhans are Gonds by historical accident and are later migrants to the Gond area from the north. The most significant and practical observation of the present study is that migration from an originally nontribal (Pardhan) to a tribal (Gond) area and admixture lead to severe disease course, differential selection pressure, and hence highly elevated HbS trait frequency.

114. Unique pattern of mutations in [beta]-thalassemia patients in Western Uttar Pradesh

2013

Indian Journal of Human Genetics

Christopher, Ajay and Kumari, Anita and Chaudhary, Sunali and Hora, Sandhya and Ali, Ziledar and Agrawal, Satish

Context: Î²-thalassemia is one of the most common heterogeneous inherited single gene disorders. The disease results from one or more of 380 different mutations in the Î²-globin gene. Uttar Pradesh (U.P.) is the most populous state of India, comprising various ethnic groups and Bareilly is one of the largest cities situated in Western U.P. Aims: To examine the prevalence of five common Î²-thalassemian mutations: Intervening Sequence IVS 1-5 (c. 92 + 5 G > C), codon 8/9 (c. 27_28insG), codon 41/42 (c. 124_127delTTCT), IVS 1-1 (c. 92 + 1 G > T) and codon 26 G-A (c. 79G > A) in Western U.P. Settings and Design: Patients attending camps organized by the Thalassemia Society, Bareilly were selected for the study. Materials and Methods: A total of 48 blood samples were collected from the patients of transfusion dependent Î²-thalassemia from July 2011 to May 2012. All the samples were analyzed for five common mutations by using the Amplification Refractory Mutation System (ARMS)-hot start-polymerase chain reaction (PCR) technique. Results: Among the five common mutations prevalent in India, we were able to detect all except codon 26 G-A (c. 79G > A), which is prevalent in northeast India. These four mutations accounted for 58% of the total number of our patients. The IVS 1-5 (G-C) was found to be the most common mutation with a frequency of 46% and the 2 nd most common mutation was Fr8/9 (+G) with a frequency of 21%. The frequency of other mutations was IVS1-1 (12%) and Cd 41/42 (4%). Conclusion: This study provides evidence that the pattern of mutations in Western U.P. is different from the rest of India and even from the neighboring states (Delhi and Punjab). To the best of our knowledge, mutation Fr8/9, the 2 nd most common mutation in our study has never been reported to be so common from anywhere in India. Some mutations, which are prevalent in other regions are absent in our region (mutation for [Epsilon]-globin). Hence, these findings can be called unique to Western U.P.

115.Mortality In Thalassemic Patients From Solapur District, Maharashtra State, India

2012

Bangladesh Journal of Medical Science

Nikam, S V and Dama, S B and Chondekar, R P and Dama, L B and Jawale, C S

Objective: The aim of the present study is to surveying the mortality in thalassemic patients from Solapur District, Maharashtra State, India. Methods: Present observational survey study, one hundred twenty five clinically proved by their medical reports, cases of thalassemic children's with age 6 months to 18 Years, coming for to get blood transfusion from different parts of Solapur district. Results: The results indicates that the increased mortality during 11-15 years of age. As a result, transfusional iron overload can cause increased morbidity and premature mortality in thalassemia patients. This study will be helpful in further defining the morbidity and mortality in thalassemic patients.

116.Sickle cell disease in tribal populations in India

2015

The Indian journal of medical research

Colah, R B and Mukherjee, M B and Martin, S and Ghosh, K

The sickle gene is widespread among many tribal population groups in India with prevalence of heterozygotes varying from 1-40 per cent. Co-inheritance of the sickle gene with Î²-thalassaemia, HbD Punjab and glucose-6-phosphate dehydrogenase (G6PD) deficiency has also been reported. Most of the screening programmes in India now use high performance liquid chromatography (HPLC) analysis although the solubility test is also sensitive and cheap. Sickle cell disease (SCD) among tribal populations is generally milder than among non-tribal groups with fewer episodes of painful crises, infections, acute chest syndrome and need for hospitalization. This has partly been attributed to the very high prevalence of Î±-thalassaemia among these tribes as well as higher foetal haemoglobin levels. However, the clinical presentation is variable with many cases having a severe presentation. There is not much information available on maternal and perinatal outcome in tribal women with sickle cell disease. Newborn screening programmes for SCD have recently been initiated in Maharashtra, Gujarat, Orissa and Chattisgarh and monitoring these birth cohorts will help to understand the natural history of SCD in India. Prenatal diagnosis is acceptable by tribal families in India. The Indian Council of Medical Research and the

National Rural Health Mission in different States are undertaking outreach programmes for better management and control of the disease.

117. Genetic epidemiology of the beta s gene.

1992

Bailliere's clinical haematology

Nagel, R L and Fleming, A F

The beta s gene arose at least four times in Africa, with three of these mutations expanding through diverse ethnic groups, but limited to definite geographical areas: Atlantic west Africa for the Senegal haplotype linked beta s; central west Africa for the Benin haplotype; and equatorial, eastern and southern Africa for the Bantu haplotype. The fourth mutation (linked to the Cameroon haplotype) is restricted to a single ethnic group, the Eton of central Cameroon. The Benin haplotype linked beta s gene was spread by gene flow to the Mediterranean (north, south and east) and to the western portions of Saudi Arabia. An independent mutation linked to a fifth haplotype, Arab-India, is found among the tribals of India (independent from their geographical origin) and in the eastern oases of Saudi Arabia. It is also suspected of being associated with the beta s gene found in Afghanistan, Iran, Transcaucasia and central Asia. The selective force involved in the expansion of the gene was most likely P. falciparum malaria, and the time of the gene frequency increase was likely to have been during the expansion of agriculture about 4000 or more years ago in India and about 3000 years ago in Africa. The partial protection against severe and life-threatening malaria is through the limitation of P. falciparum parasitaemia. This is a complex process which involves at least two mechanisms: early intraerythrocyte parasite forms are in a suicidal position through increasing the tendency of HbAS cell to sickle and then be destroyed by the spleen; intraerythrocyte growth is inhibited during deep vascular schizogony. Although there is evidence that P. falciparum (and P. malariae) parasitaemias are limited in HbSS red cells, malaria is a major trigger to haemolytic and infarctive crises in sickle-cell disease, and a common cause of morbidity and mortality.

118. Haplotypes in tribal Indians bearing the sickle gene: evidence for the unicentric origin of the beta S mutation and the unicentric origin of the tribal populations of India.

1989

Human biology

Labie, D and Srinivas, R and Dunda, O and Dode, C and Lapoumeroulie, C and Devi, V and Devi, S and Ramasami, K and Elion, J and Ducrocq, R

To determine the origin of sickle cell anemia (SS) in India, we analyzed haplotypes of the beta gene cluster in beta S-carrying individuals belonging to tribal populations living in the Nilgiris region of southern India and complemented the available data on tribes of east-central India. We found that in the Nilgiris tribes chromosomes bearing the beta S gene are linked in 91% of the cases to the "Asian" (Arab-Indian) haplotype (although 25% of the haplotypes had the epsilon polymorphic site negative, making the 5' portion of the haplotype identical with the African Senegal haplotype). These XmnI (+) chromosomes were associated with high G gamma expression (67.2 +/- 5.9%) and a high percentage of Hb F (15.5 +/- 7.9%; range, 6-25.3%). We have similar findings for tribal groups from west-central India (Gujarat). In east-central India we have confirmed the data of others, finding the same haplotype linked to beta S in tribes living in the east (Orissa, Andhra Pradesh). We conclude that the beta S gene in presently isolated and disperse tribal populations in India is associated with one predominant typical haplotype, suggesting a unicentric origin of the mutation in India. In addition, this finding implies a unicentric origin of the tribal populations themselves: The gene must have arisen and spread before tribal dispersion. Furthermore, we find extremely high frequencies of the (-alpha) haplotype in the Nilgiris (0.89) and in Gujarat (0.95). The beta S gene linkage to a high Hb F-expressing haplotype and the high incidence of alpha-thalassemia predict a mild phenotypical expression of sickle cell anemia in India.

119. Reproductive behaviour and natural selection for the sickle gene in the Baiga Tribe of Central India: The role of social parenting

1996

Annals of Human Genetics

Reddy, P H and Modell, B and Gynaecology

We have investigated the transmission of the sickle cell gene in relation to tribal structure, and genetic fitness in a primitive Indian tribal population, the Baiga. Factors operating on gene frequency include protection of AS individuals against falciparum malaria, a high frequency of genetic factors capable of moderating the severity of sickle cell anaemia (Î±-thalassaemia and Xmn 1 polymorphism in G gamma gene), a high frequency of consanguineous marriage, and reproductive compensation by couples at risk for sickle cell anaemia. The study incidentally made it possible to measure the extent of 'social parenting' in such a tribal society for the first time: deviation from expectation in the distribution of the Hb A and S genes within families suggests that up to 30% of children may not be offspring of their ostensible parents.

120. Prevalence and molecular heterogeneity of alfa+ thalassemia in two tribal populations from Andhra Pradesh, India.

1988

Human genetics

Fodde, R and Losekoot, M and van den Broek, M H and Oldenburg, M and Rashida, N and Schreuder, A and Wijnen, J T and Giordano, P C and Nayudu, N V and Khan, P M

We describe here the screening of a small group of apparently healthy individuals belonging to the tribal communities of Koya Dora and Konda Reddi. A remarkably high incidence of deletion and nondeletion alpha + thalassemia mutants has been found with allele frequencies and distributions characteristic to each tribe. We have confirmed the strict relationship between Hb S levels and the number of alpha globin genes in double heterozygotes for the S gene and alpha thalassemia. In this population sample we did not find either heterozygous carriers of alpha 0 thalassemia (deletion of both alpha genes in "cis") or individuals showing hemolytic anemia due to inactivation of three alpha-globin genes (Hb H disease). Selection by malaria is most probably responsible for the prevalence of the various alpha + thalassemia haplotypes among the two tribal populations of Andhra Pradesh.

121. Sickle cell anaemia: Epidemiology and cost of illness

2002

PharmacoEconomics

Nietert, P J and Silverstein, M D and Abboud, M R

The purpose of this paper was to review the research examining the epidemiology of and costs associated with sickle cell anaemia (SCA). Although there is general acceptance that Black populations are at greatest risk of the disease, estimates of disease incidence and prevalence vary greatly among different Black populations. In addition, the sickle cell haemoglobinopathy poses a health problem to many other ethnic groups, including populations native to Italy, Greece, Turkey, Saudi Arabia, India, Pakistan, Bangladesh, China, and Cyprus. As penicillin prophylaxis has been shown to reduce the risk of sepsis among children with SCA, many governments have established newborn screening programmes to improve the health outcomes for patients with this disease. As a group, patients with SCA incur large numbers of hospital admissions, emergency department visits, and outpatient visits, often at substantial costs, hence, obtaining adequate health insurance is a problem for many patients. A common theme present in studies reviewed in this article is that a small proportion of patients tends to account for a majority of the total healthcare costs. As new diagnostic methods and treatment options become

available, balancing costs associated with SCA and quality of healthcare will continue to present challenges to many healthcare providers and insurers.

122. Pattern of hemoglobinopathies and thalassemias in upper Assam region of North Eastern India: High performance liquid chromatography studies in 9000 patients

2014

Indian Journal of Pathology and Microbiology

Baruah, M K and Saikia, M and Baruah, A

Background: The hereditary hemoglobin (Hb) disorders are the most commonly encountered single gene disorders in India. Data pertaining to the pattern of hemoglobinopathies and thalassemias is scarce in North East India, and hence it was considered worthwhile to study these disorders using a large series of patients referred to a clinical diagnostic laboratory. Aims: A total of 9000 patients referred for Hb variant analysis were studied to identify hemoglobinopathies and thalassemias in Upper Assam region of North East India. Materials and Methods: This study was performed by high performance liquid chromatography (HPLC) using BIORAD variant Hb typing system. Results: Out of 9000 patients studied, abnormal Hb fractions were seen in 5320 patients. The HbE gene was detected in 4315 patients of which HbE trait was seen in 2294 followed by HbE disease in 1892. There were 114 HbE beta thalassemia patients and 15 double heterozygotes of HbE with HbS or HbD. Beta thalassemia trait was seen in 313 patients and beta thalassemia homozygous in 32. HbS gene was detected in 460 patients comprising of HbS trait in 189, HbS disease in 203, S beta thalassemia in 53 and double heterozygotes of SD and ES in 15. The rest comprised of HbD trait in 6, delta beta thalassemia in 33, hereditary persistence of fetal hemoglobin trait in 5 and J chain hemoglobinopathy in 8 patients. Evidence of alpha thalassemia though suspected, could not be confirmed. Conclusion: A high incidence of hemoglobinopathies and thalassemias and their combinations is unique for this part of the country.

123. Maternal and perinatal outcome of women with sickle cell disease of a tribal population in Central India

2014

Hemoglobin

Natu, N and Khandelwal, S and Kumar, R and Dave, A

Pregnancy in sickle cell disease is associated with increased risk of maternal and fetal morbidity and mortality. Sickle cell disease is very common in tribal populations. The objective of this study was to review the maternal and perinatal outcome in patients with sickle cell disease of tribal populations. This is a retrospective study. The data extracted from the patients' case files included age, gravidity, family history, complications during pregnancy or at time of delivery or postpartum period, mode of delivery, and fetal outcome. There were 25 deliveries to women with sickle cell disease and 54 with sickle cell trait. Preeclampsia and disseminated intravascular coagulation were common problems associated with sickle cell disease as compared to the sickle cell trait and normal groups. No maternal mortality occurred during the period under study. However, a total of five intrauterine fetal deaths and one early neonatal death did occur. The present study confirms the previous reports, the increased risk of fetal death in women with sickle cell disease, however, in contrast to previous studies, no maternal mortality was found. Â© 2014 Informa Healthcare USA, Inc. All rights reserved: reproduction in whole or part not permitted.

124. Association between XmnI polymorphism and HbF level in sickle cell disease patients from Chhattisgarh

2012

International Journal of Biomedical Science

Bhagat, S and Patra, P K and Thakur, A S

The Î³G-158 (Câ†'T) polymorphism plays important function in the disease severity of sickle cell anemia. The XmnI restriction site at -158 position of the Î³G-gene is associated with increased expression of the Î³G-globin gene and higher production of HbF. This study aims to determine the frequency of the different genotypes of the Î³G Xmn I polymorphism in sickle cell anemia and sickle cell trait patients in Chhattisgarh and its association with high HbF level. The Xmn1 polymorphic site was determined by PCR-RFLP procedure. XmnI polymorphism were studied in 100 sickle cell patients (SS), 50 sickle cell trait (AS) and 50 controls individuals (AA). The presence of XmnI (+/+) site in SS and AS patients associated with the increase of HbF (P<0.0001) synthesis. we also find that presence of one XmnI (+/-) site in SS patients compared with XmnI-/- site had not shows difference in HbF level. Polymorphic association is found between presence and absence of XmnI site with HbF level, in AS and AA individuals. Â© 2012 Sanjana Bhagat et al.

125. Contribution of marital distance to community inbreeding, homozygosis, and reproductive wastage for recessively inherited genetic disorders in Madhya Pradesh, India

2013

Mediterranean Journal of Hematology and Infectious Diseases

Balgir, R S

Background: Recessively inherited genetic disorders such as sickle cell anemia Î²-thalassemia are commonly encountered in heterozygous and homozygous form in India. These hemolytic disorders cause a high degree of reproductive wastage in vulnerable communities. Inbreeding is usually the mating between two related indivi process of heterosis. Purpose: This study was aimed at finding reproductive outcome in carrier couples of sickle cell anemia, and Î²-thalassemia in terms of reproductive wastage in relation to varied marital distance between partners in Madhya Pradesh. Methods: A total of 107 carrier couples, 35 and 72, respectively of cell anemia with confirmed affected offspring after taking detailed reproductive history were studied following the standard methodology in a tertiary hospital in C 2010 to February 2013. Results: A majority of sickle cell and had married within physical distance of radius less than 50 kms. away from their native places. It was found that as the marital distance between two carrier partners of above disorders decreases, the number of abortions, still-births, neonatal mortality, infant mortality, and mortality under 10 years age increases, and vice versa, implicating inbreeding and reproductive wastage of 28.2% and 18.6% was recorded in carrier couples of sickle cell disease and Î²-thalassemia, respectively. This combined reproductive wastage is negatively correlated (r= -0.74;p<0.001) to physical marital distance between the life partners. Conclusions: Relative small population size clubbed with small marital distance leads to inbreeding resulting in homozygosity which increases chances of affected offspring by recessive or deleterious traits and contributes to decreased fitness of a couple or population in Central India.

126. Haemoglobinopathies and Î²-thalassaemia among the tribals working in the tea gardens of Assam, India

2016

Journal of Clinical and Diagnostic Research

Teli, A B and Deori, R and Saikia, S P

Introduction: Prevalence of haemoglobinopathies and Î²-thalassaemia are very high in India but information about its status among the tribals working in the tea gardens of Assam is very less. Aim: The present study was carried

out to determine the prevalence of haemoglobinopathies and Î²-thalassaemia among the tribals working in the tea gardens of Assam. Materials and Methods: A total 1204 samples from the tribals working in tea gardens of Assam were analysed for both Complete Blood Count (CBC) and High Pressure Liquid Chromatography (HPLC) for detection of haemoglobinopathies and Î²-thalassaemia. Results: This study showed that the prevalence of sickle cell anaemia and Î²-thalassaemia were very high among this population. Our results indicated a higher prevalence of Î²-thalassaemia (3.07%) among the Munda ethnic group and higher prevalence of sickle cell anaemia (4.73%) among the Lohar ethnic group. This was the first study to report the presence of HbE among the tribals working in the tea gardens of Assam. Conclusion: Based on the present findings, sickle cell anaemia and Î²-thalassaemia were major health problem for the tribals working in the tea gardens of Assam. Proper diagnostic facilities for haemoglobinopathy and thalassaemia should be established in these areas, including establishment of haemoglobinopathy and thalassaemia database collection, haematological analysis laboratories, genetic counselling clinics, prenatal diagnosis centres and neonatal screening centres.

127. Prevalence of Î±+-Thalassemia in the Scheduled Tribe and Scheduled Caste Populations of Damoh District in Madhya Pradesh, Central India

2016

Hemoglobin

Singh, M.P.S.S. and Gupta, R B and Yadav, R and Sharma, R K and Shanmugam, R

This study was carried out to ascertain the allelic frequency of Î±+-thalassemia (Î±+-thal) in Scheduled caste and scheduled tribe populations of the Damoh district of Madhya Pradesh, India. Random blood samples of Scheduled tribe (267) and Scheduled caste (168), considering the family as a sampling unit, were analyzed for the presence of the â€“Î±3.7 (rightward) (NG_000006.1: g.34164_37967del3804) and â€“Î±4.2 (leftward) (AF221717) deletions. Î±+-Thal was significantly higher in the Scheduled tribals (77.9%) as compared to the scheduled caste population (9.0%). About 58.0% scheduled tribals carried at least one chromosome with the â€“Î±3.7 deletion and 20.0% scheduled tribals carried the â€“Î±4.2 deletion. Frequency for the â€“Î±3.7 allele was 0.487 in the scheduled tribal populations in comparison to 0.021 in scheduled castes. Allelic frequency for â€“Î±4.2 was 0.103 and 0.024, respectively, in the above communities. No Hardy-Weinberg equilibrium for Î±-thal gene ($p < 0.05$) was detected in the tribal population, indicating the presence of selection pressures in favor of Î±-thal mutation and adaptation.

128. Community expansion and gene geography of sickle cell trait and G6PD deficiency, and natural selection against malaria:Experience from tribal land of india

2012

Cardiovascular and Hematological Agents in Medicinal Chemistry

Balgir, R S

Malaria is globally endemic in tropical and subtropical regions and so is the hemoglobinopathies, thalassemias and glucose-6-phosphate dehydrogenase (G6PD) deficiency. This biological dogma of hyper-endemic all over the tribal land in India leads to high morbidity and mortality. The directed genetic abnormalities of human erythrocytes have found to decrease the susceptibility towards malaria parasites and the heterozygotes of abnormalities probably confer protection against the Plasmodium falciparum infection. A fascinating trend for an inverse relationship between sickle cell disorders and G6PD deficiency in scheduled caste and tribal communities of Central-Eastern India has been observed. When the frequency of sickle cell allele decreases in malaria endemic cross-section of the tribal population, the frequency of G6PD deficiency allele increases and vice versa. This medical aspect is important from an evolutionary biological background and could be an excellent point for molecular analyses to determine the signature of selection in the genomic regions of Î²-globin and G6PD genes. Since the selection favors the mutation with least cost to the population [as the clinical manifestations of G6PD deficiency are mild and do not result in a complete loss of enzyme activity against the sickle cell disease with high

morbidity and mortality in the region] and the predominant frequency of G6PD deficiency over the sickle cell disorders in some tribal communities, it seems that the replacement of sickle cell allele for G6PD deficiency is occurring in the scheduled castes/tribes of Chhattisgarh, Madhya Pradesh, Maharashtra and Odisha states in Central India. These findings are consistent with our previous studies carried out in Central-Eastern India. Â© 2012 Bentham Science Publishers.

129. Sickle cell disease: Translating clinical care to low-resource countries through international research collaborations

2018

Seminars in Hematology

Smart, L R and Hernandez, A G and Ware, R E

The vast majority of the world's population of children and adults with sickle cell disease (SCD) are born in low-resource settings, particularly in sub-Saharan Africa, the Caribbean, the Middle East, and India. As a result numerous well-established, cost-effective, and evidence-based strategies for managing SCD such as newborn screening, early education, vaccinations, screening for stroke prevention, and treatments with safe transfusions and hydroxyurea are often unavailable, leading to substantial morbidity and increased mortality. Collaborations between high-income countries and these low-resource settings (North-South partnerships) have been advocated, with the goal of improving clinical care. Based on directives promulgated by the World Health Organization, we have developed a strategy of developing prospective research programs that focus on training, capacity building, and local data collection. This strategy involves consideration of important guiding principles, full partnerships, proper planning, and financial issues before program launch, after which rigorous program management is required for full effect and long-term sustainability. Ultimately these collaborative research programs should help create national guidelines and lead to improved clinical care for all children and adults with SCD.

130. Hematological profile of sickle cell disease from South Gujarat, India

2012

Hematology Reports

Rao, S S and Goyal, J P and Raghunath, S V and Shah, V B

The aim of this study was to determine hematological profile of sickle cell disease (SCD) from Surat, South Gujarat, India. This prospective cross-sectional study was conducted in the Department of Pediatrics and Sickle Cell Anemia Laboratory, Faculty of Pathology, Government Medical College, Surat, India, between July 2009 and December 2010. Patients included in this study were in their steady state for a long period of time without any symptoms related to SCD or other diseases which could affect the hematological parameters. Venous blood of all patients was collected in ethylenediaminetetraacetic acid and hematological indices were measured. Thirty-three subjects homozygous in all were studied for their hematological parameters for sickle cell anemia. Moderate to severe anemia, low mean cell volume and high foetal hemoglobin dominate the hematological profile of SCD children. Â© S.S. Rao et al., 2012.

131. Diversity of sickle cell trait in Jharkhand state in India: Is it the zone of contact between two geographically and ethnically distinct populations in India?

2015

Journal of Biosciences

Nagar, R and Raman, R

Incidence of sickle cell trait in India is high in peninsular south, south-eastern, central and south-western India, while in north and north-eastern India, it is absent. Unicentric origin of SCD in the tribals of nilgiri hills in southern

India has been proposed. The present study on the frequency of HbS trait and Î²-globin gene haplotypes was conducted in the tribal-rich states of Chhattisgarh and Jharkhand to get an insight into the uneven distribution of HbS in India. Jharkhand borders with the HbS-high Odisha and Chhattisgarh, and HbS-low UP, Bihar and Bengal. Cellulose acetate gel electrophoresis was performed on the collected blood samples, to detect sickle haemoglobin (HbS) followed by DNA analysis. HbS associated Î²-gene haplotype was constructed for the samples positive for HbS and all the tribals by PCR-RFLP. Out of 805 (Chhattisgarh â€“ 261, Jharkhand â€“ 544; >36% tribals) samples analysed HbS frequency was 13% in Chhattisgarh and 3.3% in Jharkhand. Within Jharkhand, frequencies varied considerably from 10% in Tatanagar to nil in Sahibganj. The Arab-India (AI) haplotype of Î²-globin cluster occurred in low frequency, confined mainly to Chhattisgarh. The most abundant haplotype in all the populations was the East Asian, + â^' â^' â^' â^' +, rare in HbS, mainly in Sahibganj in east Jharkhand, which lacked AI. Our results indicate that besides the heterozygote advantage against malaria, the uneven regional distribution of HbS trait is because of restricted movement of two different populations, Dravidian from the south and Tibeto-Burman from the east into the Indian mainland which failed to meet, we conjecture, due to severe climatic conditions (deserts and heat) prevailing through parts of central India. Apparently, Jharkhand became a zone of contact between them in recent times.

132. Sickle haemoglobin, G-6PD deficiency and malaria in western Orissa.

1990

The Journal of the Association of Physicians of India

Kar, B C and Agrawal, K C and Panda, A

Sixty cases of malaria were screened for sickle haemoglobin and G-6PD deficiency. Plasmodium vivax was detected in 40 (66%) and Plasmodium falciparum in 21 (35%) cases, with six of the latter having cerebral manifestation. Sickle Hb was found in 7 (11.5%) patients and G-6PD deficiency in 3 (5%) cases. Both patients with SS disease had vivax malaria, while of 5 with sickle cell trait 3 had only vivax, one only falciparum and one mixed infection. Amongst G-6PD deficient patients one had vivax and two falciparum malaria. One of the latter had both SC trait and G-6PD deficiency. Thus, adult persons with SS disease or SC trait were not found to be resistant to either vivax or falciparum malaria. A high frequency (5%) of G-6PD deficiency amongst malaria patients warrants a caution against indiscriminate use of 8-aminoquinoline drugs.

133. Splenic syndrome due to sickle cell trait amongst Indian soldiers serving in Kashmir

2008

Medical Journal Armed Forces India

Arora, M M and Bhatia, J K and Khanna, V and Jaiswal, P and Charan, V D

Background: Heterozygous transmission of gene for Haemoglobin S leads to sickle cell trait. Mostly the trait remains silent with no additional morbidity or mortality. When these persons migrate to higher altitudes, in times of high oxygen demand, some of them develop splenic infarction. This is a rare phenomenon and only 47 such cases had been reported till 2005. Methods: This study was conducted at an Indian military hospital serving the troops deployed in Kashmir valley at altitudes ranging from 5500 ft to 13000 ft. When two consecutive splenectomies for splenic abscesses, turned out to be sickling induced infarction histopathologically, we reviewed splenectomy specimens received in last six years for evidence of sickling. Result: Out of 33 splenectomies performed during the period of study, 22 were due to trauma (gun shot injury 11; splinter injury one and blunt injury 10). Of the rest eleven, who presented without any history of trauma, seven had evidence of vascular occlusion with aggregates of sickled red blood cells. In none, Gram stain or Periodic Acid Schiff stain rrvealed any bacterial or fungal colonies. One patient of splenic syndrome was found to have unrecognised sickle cell trait and he was managed conservatively. Conclusion: Sickle cell trait should be excluded before considering splenectomy in ethnically vulnerable patients presenting with splenic syndrome. An uncomplicated splenic infarction can be managed conservatively.

134.Presence of Hb S in Uttaranchal

2007

Indian Journal of Pathology and Microbiology

Shukla, P K and Upadhyay, S and Kumar, B and Thapliyal, N and Saxena, S R and Joshi, D

Haemoglobin-S has been reported in several studies on remote populations from various parts of India eg Maharashtra, Madhya Pradesh, Andhra Pradesh, Orissa, West Bengal, Rajasthan and Malaysian Indians. Uttaranchal also has got scattered areas with people living in remote pockets due to its geophysical nature. There has been no previous report from this state about prevalence of Hb-S. In the present study on 38 individual eight were found to have Hb-S positivity by sickling test. In one of these electrophoretic confirmation was positive with demonstration of associated Beta thalassaemia. Tlte group was a family of muslims in village Bagheri near Haldwani. Due to technical, geographical and social restrictions further study could not be done. However, this study does establish the presence of Hb-S-Beta thalassaemia in Uttaranchal State for the first time. Follow up study in the affected area and elsewhere in the state might discover more of Hb-S positivity, other haemoglobinopathies and thalassaemias.

135.Haemoglobin S and Î²(Thal): Their Distribution in Maharashtra, India.

2013

International journal of biomedical science : IJBS

Urade, B P

It has been more than six decades since the first report of sickle cell anaemia in Indian subcontinent. Since then the researchers have been reported various haemoglobin varients prevalent in India, they are HbS, HbÎ²(T), HbE and HbD. Earlier studies were confined to tribal and scheduled castes populations as if sickle haemoglobin was restricted to these two groups only. Since a decade or so, few studies on haemoglobinopathies from other Indian populations are available. Examination of premarital age group of 5172 Indian subjects (2762 males and 2410 females) from eastern Maharashtra of India showed high incidences of HbS (0-33 per cent) and HbÎ²(T) (0-10 per cent) in different ethnic groups. In present study cumulative gene frequency for HbS and HbÎ²(T) was found to be of 6.1 per cent and 2.3 per cent respectively. In present study sickle cell gene has been found in general categories of Indian populations besides scheduled castes and tribal populations. In Scheduled tribes HbS ranges from 0-24 per cent, in Scheduled castes and Nomadic tribal groups, HbS ranges from 0-13 per cent, in Other Backward caste categories it varies from 0-20 per cent while in higher caste populations it ranges from 0-5 per cent. The incidences of HbS are much higher among tribal groups than that found in other caste populations. The incidences of homozygous individuals are very few in HbS and HbÎ²(T). The hitherto regional and populations specific HbÎ²(T) haemoglobin variant in Sindhi and Bengali communities is gradually spreading in other populations of Maharashtra as evident from the present study. Lesser value of MCV, MCH and MCHC in homozygous HbÎ²(T) is due to impairments of synthesis Î²-globin chain. The subject with the presence of Î²-thalassaemia is accompanied by raised level of HbA2. Unusual higher values of RBC and WBC suggest the high concentration of hypochromic microcytosis in anemia. The means of MCV MCH and MCHC in HbÎ²(T) are much lower than the normal ranges compared to HbS.

136.Sickle cell anemia associated with Î±-thalassemia in Malaysian Indians

1986

American Journal of Hematology

Lie-Injo, L E and Hassan, K and Joishy, S K and Lim, M L

The Indian rubber estate workers in Negri Sembilan, Malaysia, who originated from Orissa in India were found to have a high frequency of Hb S. Unlike the usually severe clinical picture of sickle cell anemia seen in African and American blacks, the clinical picture of the disease in this population was mild and many have reached old age. We studied the leukocyte DNA of 12 patients with sickle cell anemia, ranging in age from 4 to 61 years and 30 sickle cell trait carriers, ranging in age from 7 to 63 years, for the presence of Î±-globin gene deletions by gene mapping according to Southern, using Î±- and Î¶-globin gene probes obtained by nick translation of the Î±- and Î¶-globin genes cloned into plasmid. All 12 sickle cell anemia patients were found to have Î±-thalassemia2 (Î±-thal2), either in the homozygous or heterozygous condition. Of the Hb S trait carriers, six did not have Î±-thal2 or Î±-thal1 and 24 had Î±-thal2 (15 heterozygous, 9 homozygous). Seven of these Hb S trait carriers with Î±-thal2 had an additional gene abnormality. Five of them had a fast-moving Eco RI fragment 5.6 kb long that hybridized with Î¶-specific probe but not with Î±-specific probe. An unusual DNA pattern of a different type was further found in the other two. Bg1 II restriction analysis showed that the Î±-thal2 was mostly of the rightward delection Î±-thal2 genotype. None of the sickle cell anemia patients and Hb S trait carriers had deletion type Î±-thal1. The sickle cell anemia patients had very high levels of Hb F and low levels of Hb A2. The Hb S trait carriers with Î±-thal2 relatively low levels of Hb S.

137. The influence of faith and religion and the role of religious and community leaders in prenatal decisions for sickle cell disorders and thalassaemia major.

2006

Prenatal diagnosis

Ahmed, Shenaz and Atkin, Karl and Hewison, Jenny and Green, Josephine

OBJECTIVES: Religion is believed to have a significant impact on individuals from minority ethnic groups when making decisions about prenatal genetic screening, prenatal diagnosis and termination of pregnancy. This study aimed to explore the views of individuals from South-Asian and African-Caribbean communities towards termination of pregnancy for sickle cell disorders and thalassaemia major and the influence of (1) faith and religion, (2) perceived severity of the conditions, and (3) religious and community leaders. METHODS: The study explored the views of (1) individuals from four faith communities (Pakistani Muslims, Indian Hindus, Indian Sikhs, African-Caribbean Christians), using eight focus groups, and (2) parents of children with sickle cell disorders and thalassaemia major, using two focus groups and three interviews. RESULTS: Participants' accounts suggest that they generally considered religion and faith as an important factor in the decision-making process, but the perceived severity of the condition would play a more important role. Religious and community leaders were believed to have little role to play in the decision-making process. CONCLUSION: The findings emphasise the importance of recognising diversity within different faith groups and moving away from stereotypical views based on people's ethnicity or religion, and to consider the beliefs and preferences of individuals.

138. Can Trimodal Distribution of HbS Levels in Sickle Cell Traits Be Used To Predict the Associated Alpha-Thalassemia For Screening Cases in Central India?

2016

Iranian journal of pathology

Warpe, B M and Shrikhande, A V and Poflee, S V

BACKGROUND: Until now, trimodal distribution of HbS has been seen by six different studies in the world when associated with alpha-thalassemia with confirmation by corresponding alpha-genotyping studies. The RBC indices reduce as alpha-globin genes reduce in sickle cell trait (SCT) patients, which decreases the extent of intra-vascular sickling and thus betters the clinical course of the patients. This is a pioneer study conducted on Central Indian poor population to use the already proven six studies to screen associated alpha-thalassemia in SCT patients thus, circumventing the much costlier alpha-genotyping studies. Moreover, it aimed to study the haematological parameters in such cases. METHODS: The study was performed at RHDMC, IGGMC, Nagpur, India from 2003 to 2012. The sample population was suspected cases of haemolytic anaemia. CBC and RBC indices were obtained

by a cell analyzer. The sickle solubility test positively screened cases were confirmed by agar-gel haemoglobin electrophoresis at pH 8.6. Finally, quantitative assessment of haemoglobin variants was performed by HPLC. RESULTS: Out of total 5819 cases over ten years, 933 cases were sickle heterozygotes. Overall, 180/933 subjects were predicted to be homozygous alpha-thalassemia and 338/933 were heterozygous alpha-thalassemia, based on trimodal distribution of HbS. CONCLUSION: Genotyping is costlier for majority of the poor non-affording patients in Indian government set-ups, so this study is suitable to screen for associated alpha-thalassemia in SCT patients.

139. Sickle cell haemoglobin and glucose-6-phosphate dehydrogenase deficiency among Rellis of Visakhapatnam, Andhra Pradesh, South India.

1997

Anthropologischer Anzeiger; Bericht uber die biologisch-anthropologische Literatur

Ramesh, M and Veerraju, P

Sickle cell haemoglobin and glucose-6-phosphate dehydrogenase deficiency have been investigated in two endogamous subgroups of the Rellis, a scheduled caste population of Visakhapatnam of Andhra Pradesh (South India). The frequency for the sickle cell gene is higher among Relli-I (0.1216) than in Relli-II (0.0454). The incidence of G-6-PD deficiency is higher among Relli-II (0.0454) than in Relli-I (0.0328). The results were also compared with those available from other Andhra Pradesh populations.

140. Impact of sickle cell trait on physical growth in tribal children of Mandla district in Madhya Pradesh, India

2011

Annals of Human Biology

Qamra, S and Roy, J and Srivastava, P

Background: Reliable reports on growth impairment in sickle cell trait (SCT) children in India are lacking despite contradictory findings reported earlier. Aim: The present study assessed the impact of SCT on physical growth of tribal children of Mandla district. Subjects and methods: Weight, height, circumferences, breadths, lengths and skinfolds were recorded on 6190 children, inclusive of 732 SCT children, from birth to 12 years of age using a cross-sectional design. The sickle test was conducted in the field using 2% sodium metabisulphite followed by electrophoresis. Results: No significant difference in mean values was observed in the majority of the age groups between SCT and normal children for all 11 body measurements. However, inconsistent growth patterns in these measurements among SCT children were evident. Body weight was more deficient than height or other body measurements in the children when compared to Indian and National Centre for Health Statistics (NCHS) standards, while bicristal breadth was comparable with Indian standards. Conclusions: There was no significant impact of SCT observed on growth of children irrespective of sex. Notably, growth of SCT girls was comparable to their normal counterparts. The actual growth difference between normal and SCT children may have been masked on account of poor attainment of annual gain in each successive age group. Â© 2011 Informa UK, Ltd

141. Beta-globin gene cluster haplotypes linked to the betaS gene in western India.

2004

Hemoglobin

Mukherjee, Malay B and Surve, Reema R and Gangakhedkar, Raman R and Ghosh, Kanjaksha and Colah, Roshan B and Mohanty, Dipika

The present survey, which involves 70 sickle cell anemia patients from Gujarat and Maharashtra revealed a high prevalence of the typical Arab-Indian haplotype (91.5 %). Six atypical haplotypes, including a Cameroon one were also found. Correlation of these various haplotypes with HbF expression was studied.

142. High Prevalence of Anemia and Inherited Hemoglobin Disorders in Tribal Populations of Madhya Pradesh State, India

2020

Hemoglobin

Chourasia, S and Kumar, R and Singh, M.P.S.S. and Vishwakarma, C and Gupta, A K and Shanmugam, R

Despite estimated high prevalence of inherited hemoglobin (Hb) disorders among tribal populations in Madhya Pradesh State, India, the burden of disease is unknown, leading to high morbidity and associated mortality. Our aim was to screen tribal populations in designated tribal districts of Madhya Pradesh State for various hemoglobinopathies and to estimate the prevalence and plausible cause of anemia. The present study screened a total of 3992 tribal individuals comprised of students of Tribal schools, ashrams of Dindori, Mandla, and Chhindwara districts of Madhya Pradesh State. Screening of hemoglobinopathies was done using Hb electrophoresis and or high performance liquid chromatography (HPLC), Î±-thalassemia (Î±-thal) was detected using polymerase chain reaction (PCR). The median age of the studied cohort was 15 years (interquartile range 13â€“16 years). High prevalence (76.7%) of anemia was observed among the studied cohort. The prevalence of sickle cell trait and sickle cell disease varies from 10.7 to 15.6% and 0.4 to 0.8%, respectively. The allele frequency of sickle cell gene was highest in the Pradhan tribe followed by the Panika tribe. Dindori district had the highest prevalence of sickle cell trait. Î²-Thalassemia (Î²-thal) trait was observed in only 1.4% of the screened population. Î± Gene deletions were observed in 84.7% individuals. Significant association of Î± gene deletion mutations with mean Hb, mean corpuscular volume (MCV), and mean corpuscular Hb (MCH) was observed. The Bharia tribe showed the highest prevalence for Î±-thal. For comprehensive health care, effective intervention programs are needed to reduce the high prevalence of anemia and hemoglobinopathies among tribes.

143. Epidemiology of sickle cell disease in a rural hospital of central India.

2000

Indian pediatrics

Kamble, M and Chatruvedi, P

OBJECTIVE: To study the epidemiology of sickle cell disease in pediatric age group in a rural hospital of Central India. DESIGN: Prospective descriptive hospital based study. SUBJECTS: 99 admitted patients of sickle cell disease were studied for a period of 1 year. RESULTS: Prevalence of sickle cell disease was 5.7% (99/1753) hospitalizations of which 61.6% (n=61) had homozygous sickle cell disease (HbSS) whereas 38.4% (n=38) had heterozygous state (HbAS). Of these, 62 (63%) were below five years of age. Male : Female ratio was 1.65:1 in HbSS cases and 1.71:1 in HbAS cases. History of consanguinity was present in 7 (7%) of which 5 (8.2%) had HbSS and 2 (5.2%) had HbAS. Incidence was maximum in the Mahar community (70%) followed by Kunbi (8 %) and Teli (6%). Vascular occlusive crisis (23. 3%) was the commonest crisis encountered followed by hyperhemolytic crisis (16.3%). There was no correlation between hemoglobin levels and the occurrence of vascular occlusive crisis. Maximum cases required their first blood transfusion between second and third year of age. Requirement of blod transfusion was more in HbSS cases. Four patients died of which three had HbSS and were below five years of age. Splenic sequestration crisis was the commonest cause of death. CONCLUSION: Sickle cell disease is prevalent in this area and most cases present before 5 year of age. VOC is the commonest crisis seen, but death often occurs due to sequestration crisis and usually below 5 years of age.

144. Sickle Cell Trait Causing Splanchnic Venous Thrombosis

2015

Case Reports in Hepatology

Saxena, Priyanka and Dhiman, Pratibha and Bihari, Chhagan and Rastogi, Archana

Sickle cell trait is considered as a benign condition as these individuals carry only one defective gene and typically have their life span similar to the normal population without any health problems related to sickle cell. Only under extreme conditions, red cells become sickled and can cause clinical complications including hematuria and splenic infarction. Although twofold increased risk of venous thrombosis has been described in African Americans, there is no data available from Indian population. We here report a case of sickle cell trait from India whose index presentation was thrombosis of unusual vascular territory.

145. Influence of BCL11A, HBS1L-MYB, HBBP1 single nucleotide polymorphisms and the HBG2 XmnI polymorphism On Hb F levels.

2012

Hemoglobin

Roy, Papai and Bhattacharya, Gargi and Mandal, Amrita and Dasgupta, Uma B and Banerjee, Debasis and Chandra, Sarmila and Das, Manikanchan

In search of genetic alterations responsible for high fetal hemoglobin (Hb F) phenotypes in the population of eastern India, 91 probands were screened for four polymorphisms by sequencing and/or restriction fragment length polymorphism (RFLP) analysis. These are the A>G allele on the rs4895441 locus in the intergenic region between HBS1L and MYB on chromosome 6, the G>A allele on the rs4671393 locus on chromosome 2 (BCL11A gene), the A>C allele on the rs2071348 (HBBP1 gene) and the XmnI polymorphism (rs7482144, -158 position of HBG2) on chromosome 11. We found a significant association ($p = 0.002$ and 0.0013) of Hb F levels with rs2071348 and rs4895441, respectively. However, the polymorphism rs4671393 gene did not show significant association with Hb F levels ($p = 0.0655$). As is well known, the XmnI polymorphism ($p < 0.0001$) showed the strongest association.

146. Haemoglobinopathies in tribal populations of India

2015

Indian Journal of Medical Research, Supplement

Ghosh, K and Colah, R B and Mukherjee, M B

Haemoglobinopathies particularly haemoglobin S and E (HbS, HbE) and Î²-thalassaemia are important challenges for tribal populations in India. The HbS, HbE and Î²-thalassaemia genes are variably distributed across various tribal populations of India. HbE is mainly restricted in tribals of North-East, West Bengal, Odisha and those in Andaman and Nicobar islands. HbS has more extensive distribution in the country (10-40% trait frequency) and the homozygotes and double heterozygotes present with a wide array of morbidities. the morbidity varies greatly in different areas of the country due to differential co-inheritance of Î±-thalassaemia gene and interaction of various epistatic and environmental factors. Though substantial data on prevalence of these disorders exist, there is an urgent need to develop integrated hierarchical core facilities to manage the disease. Such centres will generate more data and will also explore areas of management which need more local attention. Newborn screening, genetic counselling, carrier detection, prenatal diagnosis along with management of cases should form the basic infrastructure of haemoglobinopathy management. Research in this areas should continue focusing on various challenges in care delivery, prevention and basic sciences on interaction of haemoglobinopathies with various other infections.

147. The Changing Trends in Prenatal Diagnosis of Hemoglobinopathies in India: The Quest of a Single Center to Reduce the Burden of Disease over Three Decades

2021

Hemoglobin

Colah, R B and Nadkarni, A H and Gorakshakar, A C and Sawant, P M and Mehta, P R and Gorivale, M S and Hariharan, P and Mohanty, D and Ghosh, K

The Î²-thalassemias and sickle cell disorders pose a considerable health burden in India. Of the more than 10,000 annual births of children with a severe hemoglobinopathy, only around 10.0% are managed optimally. Thus, genetic counseling and prenatal diagnosis (PND) is a valid option for a large and diverse country. Our center was one of the first to initiate PND and we present our experience over 30 years to evaluate the impact of awareness in changing the trends of PND of hemoglobinopathies. Both second and first-trimester diagnoses were undertaken by fetoscopy/cordocentesis and globin biosynthesis/high-performance liquid chromatography (HPLC) analysis of fetal blood and chorionic villus sampling (CVS) and DNA analysis. Over 30 years, 3478 couples (first trimester: 2475; second trimester: 1003) from all over India were offered PND. The number of couples coming in the first trimester increased significantly over each decade and couples coming prospectively increased from 2.5 to 18.4%. A cost-effective stepwise approach was used for molecular analysis. Eight hundred and one fetuses (23.0%) were affected and all except three couples opted for termination of these pregnancies. Genetic counseling and PND is the only way to reduce the burden of disease. With awareness, there was a shift from second trimester to first trimester PND over each decade, with an increasing number of couples coming during the first pregnancy. There are only 15 to 20 centers in India offering PND. We have compared our study with other reports on PND from different regions in India.

148. Compound Heterozygosity of Î²-Thalassemia and the Sickle Cell Hemoglobin in Various Populations of Chhattisgarh State, India

2018

Hemoglobin

Jha, A N and Mishra, H and Verma, H K and Pandey, I and Lakkakula, B.V.K.S.

Hemoglobinopathies evolved as a protective mechanism against malaria, which exhibit selective advantage in the heterozygous state. However, in a homozygous recessive condition, it poses a serious socioeconomic burden. Sickle cell anemia is an autosomal recessive hemoglobinopathy associated with erythrocytes sickling, vaso-occlusive crisis (VOC), as well as multi-organ failure and death. The coinheritance of other hemoglobinopathies is known to substantially modulate the clinical manifestation of sickle cell anemia. In the present study, we aimed to analyze the coinheritance of Î²-thalassemia (Î²-thal) in Hb S (HBB: c.20A>T) patients. The study includes 918 sickle cell anemia patients from 10 ethnic populations of Chhattisgarh State, India. Complete blood counts (CBCs) and hemoglobin (Hb) high performance liquid chromatography (HPLC) fractionation data were collected from patient record books. We observed Hb S-Î²-thal in all the analyzed populations. Interestingly, high frequencies of Hb S-Î²-thal have been observed in Satnami (53.8%), Rawat (47.1%), Gond (35.1%) and Panika (30.6%) populations. Inter-population comparison of hematological parameters [Hb F ($p < 0.001$), Hb A2 ($p < 0.001$), Hb ($p = 0.03$) and red blood cell distribution width (RDW) ($p < 0.001$)] revealed significant differences. We also observed that mean Hb F levels were significantly higher in Hb S compared to Hb S-Î²-thal patients in the respective populations. Our study highlights the higher prevalence of Î²-thal as well as the compound heterozygosity for Hb S and Î²-thal in various populations of Chhattisgarh State, India.

149. The frequency of the gamma chain variant A gamma T in different populations, and its use in evaluating gamma gene expression in association with thalassemia.

1985

Human genetics

Huisman, T H and Kutlar, F and Nakatsuji, T and Bruce-Tagoe, A and KilinÃ§, Y and Cauchi, M N and Romero Garcia, C

The occurrence of the A gamma T chain (i.e. A gamma 75 Ile----Thr) in different populations was evaluated through a study of 4250 cord blood samples and blood samples from more than 350 SS patients. High frequencies were observed in Italy, Yugoslavia, Turkey, Holland, but also in Japan, Vietnam, and India. The chain is (nearly) absent in the Black population of Ghana and Kenya, and low frequencies were observed in China and Australian aborigines. Only a few adult SS patients (18 out of 357) were A gamma T heterozygotes. The chromosomes with the A gamma T globin gene were mapped through an evaluation of the presence of 10 different restriction sites. The A gamma T chromosomes from different populations were closely related and had the same subhaplotypes of [- - + + T - +] (Hinc II 5' to epsilon; Xmn I 5' to G gamma; Hind III in G gamma and A gamma; Hinc II in and 3' to psi beta), quite different from the subhaplotypes seen for A gamma T negative chromosomes. This suggests a common ancestor which may have originated in Southern Europe. An evaluation of the gamma chain production by both chromosomes in SS patients and beta-thalassemia heterozygotes was possible for subjects with an A gamma T heterozygosity. It was concluded that in beta-thalassemia trait, the gamma chain synthesis is directed for about two-thirds by the thalassemic chromosome and for about one-third by the normal chromosome; the contribution by the normal chromosome decreases with a decrease in total gamma chain production.

150. Sickle cell haemoglobin, thalassaemia and g-6-PD enzyme deficiency genes in garasiya tribe inhabited malaria endemic areas of Sirohi district, Rajasthan (India)

2009

Journal of Communicable Diseases

Choubisa, S L

Venous blood samples of 368 apparently healthy and unrelated adult individuals (both male and female) belonging to a primitive tribe, Garasiya inhabitating malaria hyperendemic areas of Sirohi district, Rajasthan (India) were investigated by standard and recommended techniques for evidence of erythrocyte genetic disorders; sickle cell haemoglobin, Î²-thalassaemia syndromes and glucose-6-phosphate dehydrogenase (G-6-PD) enzyme deficiency (Gd). Sickle cell genes encountered in 23 (6.25%) Garasiya tribais. Of these, 22 (5.97%) showed heterozygous sickle cell gene(Hb-AS or trait) and one (0.27%) homozygous form (Hb-SS or sickle cell disease), Î²-thalassaemia syndromes were observed in 30(8.15%) subjects; 28(7.60%) Î²-thalassaemia traits (Î²-thal.) and 2(0.54%) HbS-thalassaemia (HbS-thal.). Gd was found in 56 (15.21 %) subjects. Except these mutant genes no other erythrocyte abnormal genes were encountered in Garasiya tribe. A high incidence or prevalence of these red cell mutant genes in relation to malaria is discussed in the present communication.

151. Prevalence of hemoglobin variants and hemoglobinopathies using cation-exchange high-performance liquid chromatography in central reference laboratory of India: A report of 65779 cases.

2018

Journal of laboratory physicians

Warghade, Sandeep and Britto, Jyothi and Haryan, Reshma and Dalvi, Tejaswi and Bendre, Rajesh and Chheda, Pratiksha and Matkar, Sunmeet and Salunkhe, Yogita and Chanekar, Milind and Shah, Nilesh

CONTEXT: Hemoglobinopathies constitute the world's most common genetically inherited red blood cell disorder. Screening and accurate identification of hemoglobin (Hb) variants have become increasingly important in antenatal diagnosis and prevention of Hb disorders. AIM: The aim of this study was to screen and identify Hb fractions prevalent in the Central Reference Laboratory of India. MATERIALS AND METHODS: A total of 65,779 cases were screened for hemoglobinopathies on the bio-rad variant high-performance liquid chromatography (HPLC) system by beta-thalassemia short program. The retention times, proportion of the hemoglobin (%) and the peak characteristics for all hemoglobin fractions were recorded. Molecular analysis of the beta-globin gene was carried out by DNA sequencing on eight cases. RESULTS: Total number of abnormal Hb fractions on cation exchange-HPLC (CE-HPLC) was seen in 12,131 (18.44%) cases. Beta-thalassemia trait was the predominant genetic Hb disorder accounting for 7377 cases (11.21%) of the total cases. This was followed by sickle cell trait (2.01%), sickle cell disease (1.59%), beta-thalassemia syndrome (0.80%), HbE trait (0.79%), and borderline HbA(2) (0.51%). Molecular characterization of eight rare cases of hemoglobin variants by beta-globin gene sequencing identified three cases of Hb Beth Israel, two cases of Hb Hofu trait, and one case each of Hb J Cambridge, Hb Mizunami, and Hb Sherwood Forest. CONCLUSION: Superior resolution, rapid assay time, and accurate quantification make CE-HPLC suitable for the routine investigation of hemoglobinopathies.

152. Prevalence of the Î²s gene among scheduled castes, scheduled tribes and other backward class groups in central India

2014

Hemoglobin

Shrikhande, A V and Arjunan, A and Agarwal, A and Dani, A and Tijare, J and Gettig, E and Krishnamurti, L

Sickle cell disease is an inherited disorder of the blood, and characterized by vasoocclusive crises (VOC), risks for pneumococcal infections and organ toxicities, is associated with morbidity and premature mortality. India, with a population of 1.2 billion individuals, is estimated to be home to over 50.0% of the world's patients with sickle cell disease. The Î²S gene [Î²6(A3)Gluâ†'Val; HBB: c.20A>T] has the highest prevalence in three socio-economically disadvantaged ethnic categories: the Scheduled Castes (SC), the Scheduled Tribes (ST), and Other Backward Class (OBC) groups in India. The tradition of endogamy practiced by the ethnic groups in India provides the rationale for the screening of individual populations to better understand the distribution of the Î²S gene, guide counseling and awareness programs and aid development of public policy. We undertook a study to describe the prevalence of the Î²S gene in these ethnic groups in the district of Nagpur, Maharashtra in Central India. Through community screening and subsequent targeted screening of high risk individuals, 35,636 individuals were screened, of whom 5466 were found to have sickle cell trait and 1010 were identified with sickle cell disease. Community screening revealed a sickle cell trait prevalence of 13.0% in the SC, 12.0% in the ST and 3.4% in the OBC population. This study describes the prevalence of the Î²S gene within these groups in Central India determined by large scale community screening. This program has uncovered previously undiagnosed cases, provided detailed information to guide population-based disease counseling, prevention and comprehensive care programs.

153. Sickle-syndromes: A study of 44 cases from Bombay

1980

Indian Pediatrics

Agarwal, M B and Mehta, B C

44 cases of sickle-syndromes were studied. 16 had homozygous sickle-cell anemia (Hb-SS, Group A), while 28 had Hb S-thalassemia (Group B). Clinically, none of the patients from Group A had a palpable spleen beyond 6 years of age, while it was palpable in all the cases of Group B irrespective of their age. Hand foot syndrome, ankle ulcerations and bleeding episodes (epistaxis) were more common in Group A. Contrary to the general belief, Hb-

A2 level failed to differentiate between the two groups. Level of fetal Hb could not be correlated with the clinical severity. Frequency of thrombotic episodes and ankle ulceration were less in comparison with the incidence described among Negroes. Some comments are made on the therapeutic aspects of various problems encountered.

154. Sickle cell disorder in aboriginal tribes of Chotanagpur

1978

Indian Pediatrics

Karan, V K and Prasad, S N and Prasad, T B

The incidence of sickle cell disorder in the aboriginal tribes of Chotanagpur has been studied. Significant number (8.3%) of positive cases were detected among the 410 cases studied. The interest of the study lies in the fact that no case of sickle cell disorder has so far been reported in the aboriginals and very few in non-aboriginals from Bihar.

155. Prevalence of hemoglobinopathies in rural Bengal, India

2012

Hemoglobin

Dolai, T K and Dutta, S and Bhattacharyya, M and Ghosh, M K

India is in the thalassemia belt of the world. Both Î±- and Î²-thalassemia (Î±- and Î²-thal) are found in West Bengal, a state in the eastern part of India. There was no systematic large published study to investigate the prevalence rates of different hemoglobinopathies in West Bengal. This study was conducted in school and college students, newly married couples and pregnant women after proper counseling in the rural areas of five districts of West Bengal state in eastern India. Thalassemia testing was done using high performance liquid chromatography (HPLC). A total of 35,413 individuals were screened for hemoglobinopathies. Î²-Thalassemia trait was found in 10.38%, Hb E [Î²26(B8)Gluâ†'Lys] trait in 4.30%, sickle cell trait in 1.12%, borderline Hb A2 value 0.73%, low Hb A2 0.68% and Hb D trait 0.37%. This is the first study that addresses the prevalence of different hemoglobinopathies in rural areas of West Bengal. The prevalence of Î²-thal trait is higher in West Bengal than other parts of India. This data is likely to be helpful in planning screening programs in rural areas of West Bengal, India. Â© 2012 Informa Healthcare USA, Inc.

156. Effect of Î±-thalassemia on sickle-cell anemia linked to he Arab-Indian haplotype in India

1997

American Journal of Hematology

***Mukherjee, M B and Lu, C Y and Ducrocq, R and Gangakhedkar, R R and Colah, R B and Kadam, M D and Mohanty, D and Nagel, R L and Krishnamoorthy*, R**

Two population groups from Western India with a high prevalence of the Î²(s) gene, one tribal (Valsad) and the other nontribal (Nagpur), were studied. The Î²(s) gene frequency in both populations was similar (0.22 vs. 0.23), but not the clinical expression of sickle-cell anemia (SS): the sickle homozygotes in the tribal group appeared to have a mild clinical course, whereas the majority in the nontribal group exhibited a more severe clinical phenotype. Both tribal and nontribal SS patients had a similarly high mean hemoglobin (Hb)F expression (18.5% vs. 15.5%) and a high number of F cells (72.3% vs. 66.6%). DNA analysis of the Î²-globin gene cluster region revealed that in these two populations, this portion of DNA was identical with and corresponded to the typical Arab-Indian haplotype. Nevertheless, in heterozygotes, the mean Î²(s) expression was lower (27.9%) in the tribal as compared to the nontribal group (35.5%). The major epistatic factor distinguishing the milder presentation in tribals vs. a more severe manifestation in nontribals was the very high frequency (0.97) of the Î²- thalassemia gene in the former as compared to the latter (0.24). We conclude that the phenotypic expression of sickle-cell anemia, linked

to the Arab- India haplotype and expressing similar levels of HbF and F cells, is not uniformly mild in India and that Î±-thalassemia is a powerful and additional epistatic factor in the Indian subcontinent.

157. A demographic prevalence of Î² Thalassemia carrier and other hemoglobinopathies in adolescent of Tharu population.

2020

Journal of family medicine and primary care

Nigam, Nitu and Kushwaha, Rashmi and Yadav, Geeta and Singh, Prithvi K and Gupta, Nitin and Singh, Bhupendra and Agrawal, Monica and Chand, Pooran and Saxena, Shailedra K and Bhatt, Madan Lal Brahma

BACKGROUND AND AIMS: Hemoglobinopathies and thalassemias are the commonest single gene disorders in India. In Terai region of India, Hemoglobinopathies and thalassemias are the most common in the Tharu community. Therefore, in this study, we aim to evaluate the Hb variant analysis of hemoglobinopathies and thalassemias in a Tharu population in Lakhimpur Kheri Districts of Uttar Pradesh, India. MATERIALS AND METHODS: Total 493 individuals were recruited in this study. The demographic details and blood samples were collected from different location at Kheri district during mega health camp. Hb variant analysis was performed by high performance liquid chromatography (HPLC) system beta thalassemia short program in BIO-RAD VARIANT. RESULTS: Out of 493, 108 (21.9%) individual suffers with abnormal haemoglobinopathies. In which Î²-thalassemia trait is the commonest haemoglobinopathy (12.98%), followed by HbE trait (7.50%), and compound heterozygous HbS/Î²-Thalassemia trait (1.42%) in overall population. The HbF was significantly greater in HbS heterozygous (1.45 Â± 1.41), whereas mean HbA2 was significantly greater in Î²-Thalassemia trait (5.17 Â± 1.36). CONCLUSION: The high incidence of hemoglobinopathies and thalassemias were observed in Tharu community in Lakhimpur Kheri districts of Uttar Pradesh, Indian.

158. Maternal mortality among tribal women at a tertiary level of care in Bastar, Chhattisgarh.

2012

Global journal of health science

Chauhan, P and Chauhan, V K and Shrivastava, P

The primary objective of this study is to study Maternal Mortality as per Gravidity among Tribal women at a tertiary level of care in Bastar, Chhattisgarh, India. Materials and This is a hospital based ,retrospective, reproductive-age mortality study (RAMOS) of tribal women of Bastar region, Chhattisgarh, that were admitted and managed in Obstetrics and Gynecology Department Govt. Medical College, Jagdalpur, Bastar, Chhattisgarh, between July 2007 and October 2011. There were total 120 cases. Results of the present study showed that among 120 deceased tribal women highest maternal mortality 65 cases (54.166%) was noted in Primigravida (Nullipara G1P0), second highest maternal mortality 44 cases (38.333%) was noted in 2nd to 4th Gravida (Multipara), 10 cases (8.333%) were in 6th and 7th Grand Multigravida (Grand Multipara), and 01 case (0.833%) was in 8th Great Grand Multigravida. Direct causes of maternal mortality were highest 46 cases (38.333%) due to hypertensive disorders of pregnancy. Among direct causes second highest 18 cases (14.999%) maternal mortality were due to Rupture Uterus, third highest 12 cases (09.999%) of Septicemia, 06 cases (04.999%) of obstructed labor, 06 (04.999%) of Hemorrhage, 02 cases (01.666%) of unsafe Abortion, 02 cases (01.666%) of Pulmonary Embolism and 01 case (0.833%) due to Aspiration. Indirect causes of maternal mortality maximum 15 cases (12.5%) of Malaria and 10 cases (08.333%) were due to Anemia and 02 cases (01.666%) were of Sickle cell Anemia. The result of the present study showed that in tertiary level of care of Bastar in the year 2007 - 2008, 2008 - 2009, 2009 - 2010 and 2010 - 2011 the total maternal deaths were 34 (n=34); 35 (n=35); 27 (n=27) and 26 (n=26) respectively. The Maternal Mortality Ratio was 1611.876; 1615.881; 1168.325 and 1000.769 Per 1, 00,000 live births in the year 2007- 2008; 2008 - 2009; 2009 - 2010 and 2010 - 2011 respectively. In the year 2007 - 2008, maternal mortality percentage among tribal women was 80.314%; in the year 2008-2009 was 85.714% and was

100% in the year 2009 - 2010 and 2010 - 2011. Discusses and/or relates this study's results to the need for improvement in the maternal health of tribal women of Bastar. It has been discussed well in the conclusion section.

159. Inherited hemoglobin disorders in Andhra Pradesh, India: A population study

2009

Clinica Chimica Acta

Munshi, A and Anandraj, M.P.J.S. and Joseph, J and Shafi, G and Anila, A N and Jyothy, A

Background: The hemoglobinopathies are a very heterogeneous group of congenital hemolytic anemias. They include thalassemias, hemoglobin variants and hereditary persistence of fetal hemoglobin. Î²-thalassemia is the most common monogenic disorder in India. Molecular characterization of this disease has revealed an extremely heterogeneous picture. Methods: 1592 blood samples from suspected cases were studied using high performance liquid chromatography, amplification refractory mutation system polymerase chain reaction and reverse dot blot techniques. Results: Out of 1592 cases, we found 119 cases of Î²-thalassemia major, and 347 cases of Î²-thalassemia trait. In addition to this, cases with structural variants like sickle cell anemia, sickle cell trait, D-thalassemia (Hb DD), E-thalassemia (Hb EE), double heterozygotes and the hereditary persistence of fetal hemoglobin were also found. Molecular analysis revealed the presence of different Î²-thalassemia mutations in the population under study. Conclusions: Molecular analysis revealed that IVS1-5(G-C) and 619Â bp deletion are the most common mutations in the population under study. The knowledge about the frequency of predominant mutations in the present population helps in offering prenatal diagnosis to the families having fetus at risk. Â© 2008 Elsevier B.V. All rights reserved.

160. Identification of therapeutic targets for inflammation in sickle cell disease (SCD) among Indian patients using gene expression data analysis.

2018

Bioinformation

Das, Ipsita and Mishra, Hrishikesh and Khodiar, Prafulla K and Patra, Pradeep K

Sickle cell disease (SCD) is life-threatening hemoglobinopathy prevalent in India, Sub-Saharan Africa and Middle East. Inflammation plays a pivotal role in disease process and involves intricate interaction among leukocytes, platelets, sickle erythrocytes and vascular endothelium. Available disease modifying therapies are hydroxyl-urea and blood transfusion. Therefore, it is of interest to develop improved pharmacological agents for SCD. We report up-regulated genes in steady state and vaso-occlusive crisis using analysis of gene expression data obtained by microarray experiment for SCD as potential targets. The association of these targets with inflammation in pathway analysis is also documented.

161. Hereditary anaemias and iron deficiency in a tribal population (the Baiga) of central India

1995

European Journal of Haematology

Reddy, P H and Petrou, M and Rddy, P A and Tiwary, R S and Modell, B

We have studied the prevalence and molecular nature of hereditary anaemias (abnormal haemoglobins, Î²-thalassaemia, Î²-thalassaemia, and Glucose 6 phosphate dehydrogenase (G6PD) deficiency) in a primitive central Indian tribe, the Baiga. 43% of the population appear to be iron-deficient. Hereditary anaemia gene frequencies are, sickle cell 0.0824, G6PD deficiency (in males) 0.0457, Î²-thalassaemia 0.0057, and deletional Î±-plus thalassaemia 0.65. Both - Î±3.7 and - Î±4.2 deletions were observed and non-deletional Î±-thalassaemia was suspected. The overall gene frequency of Xmn I + polymorphism (C â†' T - 158 cap site; upstream of G gamma region) is 0.35. This polymorphism is preferentially linked to Î²(S) genes. It appears that sickle cell disease covers a wide range of severity in the Baiga tribe based on higher mortality in the offspring of AS x AS parents

(2.5/couple) compared to AA x AS (0.75/couple) and AA x AA (0.76/couple) parents. This is compatible with the high frequency of genetic modifying factors, i.e., the Xmn I polymorphism and cl-thalassaemia. The results also indicate that 'normal' red cell values must be defined for each population where thalassaemias, G6PD deficiency and iron deficiency are common.

162. Hematological profile of sickle cell disease in central India

2007

Indian Journal of Hematology and Blood Transfusion

***Shrikhande, A V and Dani, A A and Tijare, J R and Agrawal, A* K**

Hematological profile of homozygous sickle cell disease patients attending RHDMC from Central India is presented. Central India has a huge population of sickle cell disease patients. Though predicted SS in the region is 22-44 %, 81 homozygous of sickle cell patients reported during study period of Jan 2003-Dec 2005. The clinical course of these patients is characterized in most of the cases by relatively long period without any symptoms punctuated by acute clinical events. Hematological profile of these 81 patients with age ranging from 6 month to 64 years is presented. There are 44 males and 37 females with an average age of 14.55yrs in males and 18.13 yrs females. Males out number females in pediatric age group where as females with SCD are attending hospital more in reproductive age group. Very few patients are reported after the age of 30 yrs. Average hemoglobin in males is 7.11 Â± 2.13 gms/dl and in females 6.75 Â± 1.85 gms/dl with parallel low RBC count.Hemoglobin rise is seen after 14 years of age in males and females. Age related rise in MCV is more noted in females after the age of 5 as compared to males. No age or sex related difference was seen in MCHC values. Hb A2 levels for males is 2.13 Â± 0.95% and for females 2.04 Â± 0.91 %.Hb F in males is 19.58 + 5.86% and in females is 20.99 + 4.9%. There is no age and sex related difference in Hb F levels. Moderate to severe anemia with high Hb F dominate Central Indian sickle cell disease patient's hematological profile. The hematological profile in Central India is similar to the profile in other parts of India and Saudi Arabia but different from Jamaica and Africa. Â© Indian Society of Haematology & Transfusion Medicine 2007.

163. The effect of UGT1A1 promoter polymorphism on bilirubin response to hydroxyurea therapy in hemoglobinopathies

2010

Clinical Biochemistry

Italia, K Y and Jijina, F F and Jain, D and Merchant, R and Nadkarni, A H and Mukherjee, M and Ghosh, K and Colah, R B

Objectives: Hydroxyurea is known to reduce ineffective erythropoiesis and thereby hemolysis leading to a reduction in bilirubin levels in patients with hemoglobinopathies. However, the effect of hydroxyurea on hyperbilirubinemia in relation to the UGT1A1 gene promoter polymorphism is not known in Indian patients with different hemoglobinopathies. Design and methods: We studied 112 patients (77 sickle cell anemia, 22 Î²-thalassemia intermedia and 13 HbE-Î²-thalassemia) who were on hydroxyurea therapy for 2 years for their response towards hyperbilirubinemia associated with UGT1A1 promoter polymorphism. Results: The patients with (TA)7/(TA)7 repeats had significantly higher serum bilirubin levels than those with (TA)6/(TA)6 repeats in all the groups and the reduction in serum bilirubin after hydroxyurea therapy was still higher among patients with (TA)7/(TA)7 repeats when compared with (TA)6/(TA)6 repeats. Conclusions: Higher bilirubin levels were associated with the (TA)7/(TA)7 sequence however they did not come down to normal levels after hydroxyurea therapy. Â© 2010.

164.Sickle Hepatopathy

2021

Journal of Clinical and Experimental Hepatology

Praharaj, D L and Anand, A C

Sickle hepatopathy is an umbrella term describing various pattern of liver injury seen in patients with sickle cell disease. The disease is not uncommon in India; in terms of prevalence, India is second only to Sub-Saharan Africa where sickle cell disease is most prevalent. Hepatic involvement in sickle cell disease is not uncommon. Liver disease may result from viral hepatitis and iron overload due to multiple transfusions of blood products or due to disease activity causing varying changes in vasculature. The clinical spectrum of disease ranges from ischemic injury due to sickling of red blood cells in hepatic sinusoids, pigment gall stones, and acute/chronic sequestration syndromes. The sequestration syndromes are usually episodic and self-limiting requiring conservative management such as antibiotics and intravenous fluids or packed red cell transfusions. However, rarely these episodes may present with coagulopathy and encephalopathy like acute liver failure, which are life-threatening, requiring exchange transfusions or even liver transplantation. However, evidence for their benefits, optimal indications, and threshold to start exchange transfusion is limited. Similarly, there is paucity of the literature regarding the end point of exchange transfusion in this scenario. Liver transplantation may also be beneficial in end-stage liver disease. Hydroxyurea, the antitumor agent, which is popularly used to prevent life-threatening complications such as acute chest syndrome or stroke in these patients, has been used only sparingly in hepatic sequestrations. The purpose of this review is to provide insights into epidemiology of sickle cell disease in India and pathogenesis and classification of hepatobiliary involvement in sickle cell disease. Finally, various management options including exchange transfusion, liver transplantation, and hydroxyurea in hepatic sequestration syndromes will be discussed in brief.

165.Retroperitoneal fibrosis in three siblings with the sickle cell trait.

1973

Canadian Medical Association journal

Phills, J A and Geggie, P and Hidvegi, R I and Oliva, L A

Three West-Indian black siblings with the sickle cell trait developed retroperitoneal fibrosis, a previously unreported association. Other well known renal manifestations associated with the sickle cell trait were also present in some of these cases and included renal medullary necrosis and spontaneous hematuria. It is postulated that the sickling of the erythrocytes in the periureteral vessels resulted in thrombosis, ischemia, reactive scarring and progressive fibrosis indistinguishable from the known histological picture of retroperitoneal fibrosis. The finding of fibrin thrombi in the small veins of the fibrotic tissue of one of these patients would support this explanation.

166.Biochemical indicator of sickle cell disease: Preliminary report from India

2012

Indian Journal of Clinical Biochemistry

Pandey, S and Sharma, A and Dahia, S and Shah, V and Sharma, V and Mishra, R M and Pandey, Sw. and Saxena, R

Blood biochemistry has significant effect on pathophysiology of human body. Recently few studies found the association of biochemical abnormalities in sickle cell patients. Sickle cell disease showed clinical variability where African ancestors have severe phenotype than Indian sicklers. Our aim was to evaluate the bio-chemicals in sickle cell patients and their effect on severity. Here we present the comparative biochemical levels in sickle

cell patients as well as controls. Sickle cell patients diagnosed by HPLC and biochemical analysis done by Beckman-auto analyzer. T test applied for statistical analysis. Result showed the renal abnormality lesser in patients and related biochemical within the normal range and statistically not significant. Electrolytes, hepatic enzymes, alkaline phosphatase and glucose were elevated and statistically significant (P value <0.05). Observation of the study concludes the biochemical abnormality play a significant role in sickle cell patient's physiopathology and can be used to management of the disease. Â© 2012 Association of Clinical Biochemists of India.

167.Sickle cell anemia and trait in a population of Southern India

1977

American Journal of Hematology

Brittenham, G and Lozoff, B and Harris, J W

In an ethnic group in southern India, the Irula, seven individuals with sickle cell anemia were found to manifest only mild illness. Although a relatively high level of fetal hemoglobin was present in one, none of the factors thought to ameliorate the course of sickling disorders could be identified in the remaining six. In a random population survey, sickle hemoglobin was found in 90 of 292 Irula (31%). In those with sickle cell trait, the proportion of sickle hemoglobin in hemolysates (mean = 26%, range 19-32%) was substantially than that reported for any other population.

168.Morbidity pattern in hospitalized under five children with sickle cell disease

2013

Indian Journal of Medical Research, Supplement

Jain, D and Bagul, A S and Shah, M and Sarathi, V

Background & objectives: Children with sickle cell disease require more frequent hospital care and younger children (<5 yr of age) are more vulnerable to mortality. There are limited data on the events leading to hospitalizations and death in younger children with sickle cell disease from India. This study was, therefore, undertaken to evaluate the morbidity pattern in hospitalized under five children with sickle cell disease in a tertiary care hospital in Maharashtra, India. Methods: This was a prospective observational study carried out from July 2007 to June 2009. Hospitalized children below five years of age with sickle cell disease were enrolled for the study and evaluated for morbid event/s leading to hospitalization. Haematological indices were noted at baseline (most recent past when patient was not acutely sick) and at the time of hospitalization. Results: Eighty five children with sickle cell disease were hospitalized during the study period. Hospitalization with acute febrile illness (31%) was the most common morbid event followed by severe anaemia (30%) and acute painful events (20%). Majority (62%) of the events occurred between August and October. Forty five patients had foetal haemoglobin (HbF) more than 20 per cent (26.80Â±4.81%) and morbidity was significantly less in these patients. Interpretation & conclusion: Acute febrile illness was the most common morbid event followed by severe anaemia and acute painful event hospitalized children with sickle cell disease. There was significant seasonal variation with maximum events occurring in the monsoon season.

169.Splenic Infarct on Exposure to Extreme High Altitude in Individuals with Sickle Trait: A Single-Center Experience

2019

High Altitude Medicine and Biology

Kumar, R and Kapoor, R and Singh, J and Das, S and Sharma, A and Yanamandra, U and Nair, V

Background: Sickle cell trait (SCT) is a common genetic abnormality in the so-called "sickle belts" in India. Splenic infarction often brings to medical attention an underlying SCT, when appropriately looked for. The hypoxic environment of an extreme high-Altitude area (HAA) is conducive for developing a splenic infarct in an SCT individual not a native of these areas. Aims: We studied retrospectively 27 cases who presented with a splenic infarction during the last 4 years. Results: Twenty-five patients (92.5%) were diagnosed to have SCT, and 85% patients had developed splenic infarct on exposure to very HAAs. Clinically, splenomegaly was seen in 33% of patients with splenic infarct at presentation. The mean hemoglobin S was 36.92% in SCT individuals. A thrombus in the splenoportal axis was demonstrated in 22.2% of cases. Splenic rupture was a rare event, seen in only 3.5% of patients. Splenectomy was not required in any of the cases. Splenic abscess was not seen, and antibiotics were not required in any of the cases. We discuss the profile and management of these patients and review the literature on splenic infarction in HAA. Conclusion: SCT is commonly overlooked cause of splenic infarction and conservative management is effective in most of the cases. Splenectomy is required only in the rarest of rare cases. The profile and management of these patients and a review of the literature on splenic infarction in HAA has been discussed.

170. The spatial epidemiology of sickle-cell anaemia in India

2018

Scientific reports

Hockham, C and Bhatt, S and Colah, R and Mukherjee, M B and Penman, B S and Gupta, S and Piel, F B

Sickle-cell anaemia (SCA) is a neglected chronic disorder of increasing global health importance, with India estimated to have the second highest burden of the disease. In the country, SCA is particularly prevalent in scheduled populations, which comprise the most socioeconomically disadvantaged communities. We compiled a geodatabase of a substantial number of SCA surveys carried out in India over the last decade. Using generalised additive models and bootstrapping methods, we generated the first India-specific model-based map of sickle-cell allele frequency which accounts for the district-level distribution of scheduled and non-scheduled populations. Where possible, we derived state- and district-level estimates of the number of SCA newborns in 2020 in the two groups. Through the inclusion of an additional 158 data points and 1.3 million individuals, we considerably increased the amount of data in our mapping evidence-base compared to previous studies. Highest predicted frequencies of up to 10% spanned central India, whilst a hotspot of ~12% was observed in Jammu and Kashmir. Evidence was heavily biased towards scheduled populations and remained limited for non-scheduled populations, which can lead to considerable uncertainties in newborn estimates at national and state level. This has important implications for health policy and planning. By taking population composition into account, we have generated maps and estimates that better reflect the complex epidemiology of SCA in India and in turn provide more reliable estimates of its burden in the vast country. This work was supported by European Union's Seventh Framework Programme (FP7//2007-2013)/European Research Council [268904 - DIVERSITY]; and the Newton-Bhabha Fund [227756052 to CH].

171. Screening for the sickle cell gene in Chhattisgarh state, India: An approach to a major public health problem

2011

Journal of Community Genetics

Patra, P K and Chauhan, V S and Khodiar, P K and Dalla, A R and Serjeant, G R

The aim of this study is to determine the feasibility of large-scale population screening for the sickle cell gene in high risk areas with limited resources. A programme designed to detect the sickle cell trait and sickle cell disease has screened 359,823 subjects among 2,087 (99.7%) of the villages in Raipur District, Chhattisgarh State, India between October 2007 and June 2010. Children aged 3-15 years were initially screened in the villages by solubility

tests on fingerprick samples. Venipuncture was performed on subjects with positive solubility tests, and the samples were transferred to Raipur Medical College for alkaline haemoglobin electrophoresis. The sickle cell trait occurred in 33,467 (9.30%) and an SS phenotype in 747 (0.21%). The gene frequencies were not in Hardy-Weinberg equilibrium most likely due to a deficiency of the SS phenotype failing to enter the sampled population from either sickness or early death. Subjects with abnormal haemoglobin genotypes may factor this information into decisions regarding marriage and avoid the risks of having children with sickle cell disease. The techniques described may be a model for other developing societies with limited resources. Â© Springer-Verlag 2011.

172.Microalbuminuria as a predictor of early glomerular injury in children with sickle cell disease

2003

Indian Journal of Pediatrics

Datta, V and Ayengar, J R and Karpate, S and Chaturvedi, P

Objective: A cross sectional study was carried out to determine the prevalence of microalbuminuria in the pediatric patients with sickle cell disease. Methods: The study was carried out on 64 pediatric patients aged less than 14 years with documented HbSS, HbAS and HbS beta thalassemia, Microalbuminuria was estimated using single radial immuno diffusion technique. Majority of the study subjects were of HbSS type. 38.5% had symptoms for >2 years. 18.8% of the study population had significant microalbuminuria (19.2% of SS types and 18.8% of Hb AS types). Result: Microalbuminuria excretion was significantly more in patients >9 years of age as compared to young patients ($p<0.05$). Mean serum creatinine levels did not show any significant difference in the various study groups. Conclusion: Microalbuminuria estimation is a very important clinical marker of preclinical glomerular damage in patients with sickle cell disease. Its estimation would help in the early detection of such patients and prompt initiation of therapy.

173.Spectrum of haemoglobinopathies in a tertiary care hospital of armed forces

2008

Medical Journal Armed Forces India

Chopra, G S and Nair, V and Gupta, P K and Mishra, D K and Sharma, A and Mathew, O P

Background: Thalassaemia and other structural haemoglobinopathies are the major genetic disorders prevalent in certain parts of the world including India. This study presents the pattern of haemoglobinopathies amongst the referred patients of anaemia in a two-year period. Methods: A total of 1032 patients were studied during a two-year period for anaemia investigation. Haematological indices, sickling test and haemoglobin electrophoresis with quantification of the bands was done in all cases. Result: Out of 1032 cases, 774 (75%) were normal and 258 (25%) cases had abnormal haemoglobin pattern. Of the 258 abnormal cases, 136 (53%) were males and 122 (47%) were females. Of all cases of anaemia 370 (36%) were microcytic hypochromic, 237 (23%) macrocytic, 151 (15%) were dimorphic and the rest (26%) had normocytic normochromic picture. 82% of microcytic hypochromic anaemias had reduced serum iron and elevated total iron binding capacity (TIBC), whereas 85% had decreased serum ferritin levels. Spectrum of haemoglobinopathies prevalent were Î²-Thalassemia trait (17%), followed by sickle cell trait (2.3%). Other haemoglobinopathies in descending order of frequency were sickle cell disease (1.7%), Hb D trait (1%), Hb E trait (0.8%), sickle cell - Î² thalassemia, Hb E disease, E - Î² thalassemia (0.6% each) and thalassemia major (0.4%). Conclusion: This study provides a comprehensive database on the spectrum of haemoglobinopathies in the Armed Forces. It is suggested that detection of HbA2 should be carried out in all the high-risk groups with anaemia.

174. Haptoglobin polymorphism among the tribal groups of southern Gujarat

2011

Indian Journal of Human Genetics

Khurana, P and Aggarwal, A and Huidrom, S S and Kshatriya, G K

Background : Gujarat is located at the western most point of the Indian subcontinent. Valsad and Surat districts are part of the 'tribal belt' of Gujarat and constitute 29.1% of total tribal population of Gujarat. These tribal populations are a rich source of gaining insights in the patterns of genetic diversity and genetico-environmental disorders against the back drop of their ecological, historical and ethnographic aspects. Aim : The objectives were to find out a) the genetic diversity among the tribes of Gujarat with reference to haptoglobin (Hp) locus b) the relationship between Hp polymorphism and sickle cell anemia/trait. Materials and Methods: 431 individuals belonging to eight tribal groups were studied for Hp polymorphism using polyacrylamide disc gel electrophoresis (PAGE). HbFNx01S was screened by dithionate tube turbididy (DTT) test and confirmed using cellulose acetate membrane electrophoresis (CAME). Statistical Analysis: Allele frequency was calculated by direct gene counting method. Average heterozygosity and gene diversity were computed using software DISPAN. Analysis of molecular variance (AMOVA) was estimated using software ARLEQUIN version 3.1. Results and Conclusions: Pattern of allele frequency distribution showed preponderance of Hp 2 allele in all the eight tribal groups, which is in accordance with its frequency in different populations of Indian subcontinent. Total average heterozygosity (H T) was found to be low (0.160) but the level of genetic differentiation (G ST) was found to be moderately high (5.6%). AMOVA analysis indicated least among group variance between west and south Indian populations (-0.04%) indicating the affinities of the tribes of Gujarat with that of Dravidian speaking groups. Analysis of Hp phenotypes among sickle cell anemia/ trait individuals revealed a high frequency of Hp 0-0 phenotype (92.7%) among SS individuals as opposed to only 9.7% among AS individuals, reaffirming the selective advantage of HbAS state in relation to hemolytic disorders.

175. Haemoglobinopathies in India: estimates of blood requirements and treatment costs for the decade 2017â€“2026

2020

Journal of Community Genetics

Sinha, S and Seth, T and Colah, R B and Bittles, A H

The Government of India is presently engaged in the implementation of a prevention and control programme for two major forms of haemoglobinopathies, thalassaemia major and sickle cell disease, with guidelines for their prevention and management formulated under the National Health Mission. Based on projections for the population up to the year 2026, the annual blood requirement for treatment will increase to 9.24 million units, together with an 86% increase in budgetary requirements which then would account for over 19% of the current National Health Budget. To avert a public health crisis there is an urgent need to fully implement the prevention programme for haemoglobinopathies.

176. Clinico-haematological profile of hereditary haemolytic anaemias in a tertiary health care hospital in South India

2017

Journal of Clinical and Diagnostic Research

Venkataswamy, C and Shanthala Devi, A M

Introduction: Hereditary haemolytic anaemia is a common inherited disorder causing varying degree of morbidity and mortality. This includes disorders due to haemoglobin defect, membrane defect, and enzyme defect. Among them haemoglobinopathies, a single gene disorder, constitutes the major part of the disorder and is distributed worldwide with an incidence of 5%. These inherited disorders pose a major public health problem and increase

the burden both on the patient and the society. Presently, these disorders are not curable but can only be prevented. Improved awareness about these diseases among medical fraternity leading to diagnosis of carrier state, genetic counselling, and antenatal diagnosis may help in decreasing the prevalence of the disease. Aim: To determine the prevalence of hereditary haemolytic anaemia and to correlate clinical and haematological features. Materials and Methods: The study was carried for duration five and half years (four years of retrospective and one and a half years prospective). All the patients diagnosed as hereditary haemolytic anaemia based on peripheral smear and special haematological investigation were included in the study. The clinical parameters and haematological parameters of all these patients were studied. Results: A total of 322 cases of hereditary haemolytic anaemia were diagnosed over a period of five and a half years. Of them thalassaemia syndrome constituted 165 cases (51.24%), sickle cell disorders 78 cases (24%), hereditary spherocytosis 43 cases (13.3%), G6PD deficiency 20 cases (6.29%) and HbE disorder 12 cases (3.7%). One case of hereditary elliptocytosis and one case of HbD Punjab was detected. Among thalassaemia syndromes beta thalassaemia was commonest clinically presenting disorder with a high morbidity. Sickle cell anaemia showed a higher level of HbF and a relatively milder clinical course. Hereditary spherocytosis had varied age at presentation. In G6PD deficiency drug induced haemolysis was the commonest clinical presentation. HbE disorders were from the north eastern states. Conclusion: Haemoglobinopathies constitute the major group of hereditary haemolytic anaemia (74%). Genetic counselling is an important step in reducing the incidence of thalassaemia major.

177. Some atypical and rare sickle cell gene haplotypes in populations of Andhra Pradesh, India

1999

Human Biology

Niranjan, Y and Chandak, G R and Veerraju, P and Singh, L

We have investigated the clinical, hematological, and molecular genetic characteristics of sickle cell anemia patients from 6 populations of Andhra Pradesh, South India. Of 72 sickle cell chromosomes (HBB*S) 60 belong to characteristic Arab-Indian haplotypes, 6 to variant Arab-Indian haplotypes, 1 to a Bantu haplotype, 2 to a Cameroon haplotype, and 3 to rare haplotypes. This is the first report of a Bantu haplotype in an Indian population. Some information on haplotype characteristics of normal chromosomes (HBB*A) is also presented. The average hemoglobin level was 7.3 g% and mean fetal hemoglobin (HbF) level was 12.6%. The higher HbF levels corroborate earlier observations in sickle cell homozygotes from India. Clinical investigations have revealed splenomegaly and painful crises as the most common features in these patients.

178. Sickle cell anemia and trait in southern India: Further studies

1979

American Journal of Hematology

Brittenham, G and Lozoff, B and Harris, J W

Population surveys and family studies among 568 members of nine ethnic groups in southern India identified 15 homozygotes for sickle hemoglobin (Hb S) who had mild clinical and hematological manifestations with high levels of fetal hemoglobin (mean = 20%, range 8-36%) in a heterogeneous red cell distribution. In one family, the heterozygous mother had a hemoglobin pattern consistent with a form of the heterocellular hereditary persistence of fetal hemoglobin. Sickle cell trait was found in 153 (27%) of those studied. Chromatographic quantitation of the hemoglobin fractions in these heterozygotes showed a trimodal distribution of the proportion of Hb S explicable by a genetic model postulating the presence of genotypes with two (-Î±/-Î±), three (-Î±/Î±Î±) and four (Î±Î±/Î±Î±) active Î±-globin genes. Globin synthesis studies in four heterozygotes believed to have two active Î±-globin genes demonstrated an Î±/non-Î± total activity ratio (0.57) consistent with this model.

179.Burden of genetic disorders in India.

2000

Indian journal of pediatrics

Verma, I C

India, like other developing countries, is facing an accelerating demographic switch to non-communicable diseases. In the cities congenital malformations and genetic disorders are important causes of morbidity and mortality. Due to the high birth rate in India a very large number of infants with genetic disorders are born every year almost half a million with malformations and 21,000 with Down syndrome. In a multi-centric study on the causes of referral for genetic counselling the top four disorders were repeated abortions (12.4%), identifiable syndromes (12.1%), chromosomal disorders (11.3%) and mental retardation (11%). In a more recent study in a private hospital the top reasons for referral were reproductive genetics (38.9%)--comprising prenatal diagnosis, recurrent abortions, infertility and Torch infections--mental retardation +/- multiple congenital anomalies (16.1%), Down syndrome (9.1%), thalassemia/haemophilia (8.8%), and muscle dystrophy/spinal muscular atrophy (8.4%). The disorders for which prenatal has been done over an 18-month-period are given. A recent study carried out in three centers (Mumbai, Delhi and Baroda) on 94,610 newborns by using a uniform proforma showed a malformation frequency of 2.03%, the commonest malformations are neural tube defects and musculo-skeletal disorders. The frequency of Down syndrome among 94,610 births was 0.87 per 1000, or 1 per 1150. Screening of 112,269 newborns for aminoacid disorders showed four disorders to be the commonest--tyrosinemia, maple syrup urine disease and phenylketonuria. Screening of cases of mental retardation for aminoacid disorders revealed four to be the commonest--hyperglycinemia, homocystinuria, alkaptonuria, and maple syrup urine disease. Metabolic studies of cases of mental retardation in AIIMS, Delhi and KEM Hospital, Mumbai, demonstrated that common disorders were those of mucopolysaccharides, lysosomes, Wilson disease, glycogen storage disease and galactosemia. It is estimated that beta- thalassemia has a frequency at birth of 1:2700, which means that about 9,000 cases of thalassemia major are born every year. Almost 5200 infants with sickle cell disease are born every year. Disorders, which deserve to be screened in the newborn period, are hypothyroidism and G-6-PD deficiency, while screening for aminoacid and other metabolic disorders could presently be restricted to symptomatic infants.

180.Î²-Globin haplotype analysis suggests that a major source of Malagasy ancestry is derived from Bantu-speaking Negroids

1996

American Journal of Human Genetics

Hewitt, R and Krause, A and Goldman, A and Campbell, G and Jenkins, T

The origins of the inhabitants of Madagascar have not been fully resolved. Anthropological studies and preliminary genetic data point to two main sources of ancestry of the Malagasy, namely, Indonesian and African, with additional contributions from India and Arabia. The sickle-cell (Î²(S)) mutation is found in populations of African and Indian origin. The frequency of the Î²(S)-globin gene, derived from 1,425 Malagasy individuals, varies from 0 in some highland populations to .25 in some coastal populations. The Î²(S) mutation is thought to have arisen at least five times, on the basis of the presence of five distinct Î²(S)-associated haplotypes, each found in a separate geographic area. Twenty-five of the 35 Malagasy Î²(S) haplotypes were of the typical 'Bantu' type, 1 'Senegal' haplotype was found, and 2 rare or atypical haplotypes were observed; the remaining 7 haplotypes were consistent with the Bantu haplotype. The Bantu Î²(S) mutation is thought to have been introduced into Madagascar by Bantu-speaking immigrants (colonists or slaves) from central or east Africa. The Senegal Î²(S) mutation may have been introduced to the island via Portuguese naval explorers. This study provides the first definitive biological evidence that a major component of Malagasy ancestry is derived from African populations, in particular, Bantu- speaking Negroids. Î²(A) haplotypes are also consistent with the claim for a significant African

contribution to Malagasy ancestry but are also suggestive of Asian/Oceanic and Caucasoid admixture within the Malagasy population.

181. Sickle cell haemoglobin and glucose-6-phosphate dehydrogenase deficiency among Dhobis of Visakhapatnam, Andhra Pradesh, India.

1993

Anthropologischer Anzeiger; Bericht Ã¼ber die biologisch-anthropologische Literatur
Ramesh, M and Balakrishna, A and Veerraju, P

Sickle cell haemoglobin and glucose-6-phosphate dehydrogenase deficiency are reported for Dhobis, a washerman caste population of Visakhapatnam city, Andhra Pradesh, India. The results are compared with those of other caste populations from Andhra Pradesh.

182. The prevalence of factor V Leiden (G1691A) and methylenetetrahydrofolate reductase C677T mutations in sickle cell disease in Western India

2015

Clinical and Applied Thrombosis/Hemostasis

Kangne, H K and Jijina, F F and Italia, Y M and Jain, D L and Nadkarni, A H and Ghosh, K K and Colah, R B

The prevalence of the Factor V Leiden (FVL; G1691A) mutation and the methylenetetrahydrofolate reductase (MTHFR; C677T) mutation was determined in 180 patients with sickle cell (SS) disease (126 sickle homozygous and 54 sickle Î²-thalassaemia - age 1-47 years) and in 130 healthy controls. The FVL mutation in the heterozygous state was present in only 3 patients with SS disease and was absent in the controls. Genotyping of MTHFR 677C > T revealed increased frequency of the C allele than the T allele in patients as well as in controls. This suggests that these genetic markers may not be major risk factors for a hypercoagulable state in Indian patients with SS disease.

183. Hemoglobinopathies in South Gujarat population and incidence of anemia in them

2012

Indian Journal of Human Genetics

Patel, A and Shah, A and Sorathiya, S and Gupte, S

Objective: To Screen of South Gujarat population for determination of prevalence of different hemoglobinopathies particularly beta thalassemia trait (BTT) and sickle cell trait (SCT) and find out the incidence of anemia in them. Material and Methods: The present study screened 32,857 samples of students from different school and colleges in South Gujarat. Blood samples were initially tested for solubility test and complete hemogram on hematology analyzer. Samples having MCV (â‰¤78), MCH (â‰¤28) and/or positive solubility test were investigated for Hb electrophoresis on cellulose acetate membrane (pH 8.6). Hb A2 level â‰¥3.5% was considered as diagnostic for BTT. High performance liquid chromatography on Biorad Hb variant system was done on samples having doubtful results. Result: Overall prevalence of BTT and SCT in South Gujarat was 4.4% and 1.3% respectively. Gamit, Vasava, Chaudhary, and Mahyavanshi castes had high prevalence of BTT (15.9%, 13.6%, 12.6%, and 6.9%) as well as SCT (22.2%, 15.2, 22.3, and 4.2%) respectively. Other communities like Lohana (10.8%), Sindhi (10.2%), Prajapati (6.3%), and Ghanchi (6.2%) also showed higher prevalence of BTT. Incidence of mild to moderate anemia was higher in BTT and SCT compared to non-BTT or non-SCT subjects. Conclusion: Study suggests that BTT is the most prevalent hemoglobinopathy in South Gujarat. Î²-thalassemia and Sickle cell anemia are highly prevalent in Mahyavanshi, Chaudhary, Gamit, Vasava and Rohit. Prajapati, Lohana, Leva Patel, and Ghanchi have Î²- thalassemia risk. SCT is more frequently detected in Dhodia Patel and Kukanas. Copyright Â© 2012 Indian Journal of Human Genetics.

184. The burden of genetic disorders in India and a framework for community control

2002

Community Genetics

Verma, I C and Bijarnia, S

With a very large population and high birth rate, and consanguineous marriage favoured in many communities, there is a high prevalence of genetic disorders in India. An estimated 495,000 infants with congenital malformations, 390,000 with G6PD deficiency, 21,400 with Down syndrome, 9,000 with Î²-thalassaemia, 5,200 with sickle cell disease, and 9,760 with amino acid disorders are born each year. The prevalence of late-onset multi-factorial disorders (including coronary artery disease, hypertension and psychiatric disorders) is also large. Due to inadequate diagnostic, management and rehabilitation facilities, the burden of these disorders is greater than in Western countries. Although genetic diseases receive little attention from the health services, research funding by the government has been liberal. Community control of common disorders like thalassaemia, Down syndrome, neural tube defects, and muscular dystrophies deserves high priority, and genetic services should be integrated into the existing primary health care and medical services. Most genetic counselling would have to be provided through training physicians who staff the district and medical school hospitals. To ensure future progress, there is a need to establish additional departments of medical genetics in medical schools. Copyright Â© 2002 S. Karger AG, Basel.

185. Cell disease in Central India

2004

Indian Journal of Pediatrics

Patel, A B and Athavale, A M

Objective: The incidence and the risk factors of sickle cell disease (SCD), vaccinated with Pneumococcal vaccine and on penicillin prophylaxis has not been previously reported in India. Methods: This prospective hospital based study followed 325 children on penicillin prophylaxis, of which 161 were vaccinated for pneumococci, over 146.84 person years to determine the incidence and determinants of crisis (SCC) and infections. The average age at presentation was 7.05 Â± 3.26 years with male preponderance below 2 years. Results: The main causes for hospitalizations were for blood transfusion, SCC and infections. The incidence of SCC was 1.25 per patient per year and that of infection was 1.38 per person per year. The risk factors for SCC were Mahar caste (p = 0.007) non-compliance (p = 0.000) and protein energy malnutrition (PEM) (p = 0.0015) and for infection were also PEM (p = 0.023), Mahar caste (p = 0.021) and noncompliance (p = 0.001). Conclusion: Malnutrition and non-compliance with medication increased the patient's susceptibility to SCC and infections.

186. Sickle cell disease in Madhya Pradesh, Central India: A comparison of clinical profile of sickle cell homozygote vs. sickle-beta thalassaemia individuals

2016

Hematology

Yadav, R and Lazarus, M and Ghanghoria, P and Singh, M.P.S.S. and Gupta, R B and Kumar, S and Sharma, R K and Shanmugam, R

Background and objectives: The clinical manifestation in sickle cell disease (SCD) patients varies from one individual to another due to factors like the presence of alpha-thalassaemia mutation, foetal haemoglobin, and Î²-globin gene haplotype. The present study enumerates the clinical profile of sickle cell anaemia patients from Central India. Methods: Seven hundred seventy-six SCD patients from Jabalpur and surrounding districts (Madhya Pradesh) in central India were registered with the sickle cell clinic of NIRTH, Jabalpur. The present study reveals recorded signs and symptoms of genetically confirmed sickle cell anaemia (404) and sickle beta thalassaemia (92) patients. Results: Majority of the patients were from scheduled caste communities (47.9%) and

Gond tribal community (13.8%). Splenomegaly was the most common clinical manifestation observed (71.4%). Overall, 63.5% patients had a history of blood transfusion. The most frequent signs and symptoms observed were Pallor, Icterus, Joint pain, Fever, and Fatigue. Majority of the patients revealed onset of disease prior to attaining the age of 3 years (sickle cell anaemia 44.3% and sickle beta thalassaemia 35.9%). Mean haemoglobin levels among SCA individuals were marginally higher than SBT patients. On the other hand, mean foetal haemoglobin levels among SBT individuals showed the reverse trend. Notably, the present study reports the first incidence of priapism recorded in Central India. Conclusions: The study revealed a high prevalence of SCD among scheduled caste, backward caste, and tribal communities. Dissemination of study findings, screening, pre-marriage counselling, and pre-natal diagnosis are fundamental to preventing or lowering of birth of sickle cell anaemia children in the affected populations.

187. Sickle cell anemia from central India: A retrospective analysis

2012

Indian Pediatrics

Jain, D and Italia, K and Sarathi, V and Ghoshand, K and Colah, R

Although sickle cell anemia in India is believed to have a mild clinical presentation, few studies report severe disease in many patients from central India. Hence, we have retrospectively studied 316 children with SCA who were followed up for a period of 5.8Â±5.7 years. There were 55.4 blood transfusions, 43.3 episodes of vaso-occlusive crises requiring hospitalization, and 108.9 hospitalizations per 100 person years. Ninety six (30%) patients had severe disease whereas 74 patients also fulfilled the criteria for hydroxyurea therapy. Significant proportion of children with sickle cell anemia from central India present with severe clinical presentation and require regular medical attention. Â© 2012 Indian Academy of Pediatrics.

188. Prevalence of factor v Leiden G1691A, MTHFR C677T, and prothrombin G20210A among Asian Indian sickle cell patients

2012

Clinical and Applied Thrombosis/Hemostasis

Pandey, S K and Meena, A and Kishor, K and Mishra, R M and Pandey, S and Saxena, R

The prevalence of factor V (FV) Leiden G1691A, prothrombin G20210A, and methylenetetrahydrofolate reductase (MTHFR) C677T mutations were investigated among 90 sickle trait, 61 sickle homozygous, 75 sickle beta thalassemia, and 15 HbSD Asian Indian sickle cell patients. In all, 297 healthy controls were evaluated to compare the polymorphism frequency. The prevalence of FV Leiden heterozygous G>A were significant in the group (P =.02), while PRT G20210A polymorphism was not seen among patients as well as controls. However, an increased frequency of the MTHFR 677 C>T genotype was seen among patients as well as controls, but this was not statistically significant (P =.13). This suggested a low impact of inherited hypercoagulability risk factors in the pathogenesis of sickle cell disease and/or its complications. Â© 2012 The Author(s).

189. Spectrum of sickle cell diseases in patients diagnosed at a tertiary care centre in karnataka with special emphasis on their clinicohaematological profile

2016

Journal of Clinical and Diagnostic Research

***Lokanatha, H and Rudramurthy, P and Ramachandrappa, R M* G**

Introduction: Sickle cell disease is a monogenic disorder with considerable clinical diversity and Sickle haemoglobin is responsible for wide spectrum of disorders which vary with respect to severity of anaemia, frequency of crises and duration of survival. As they are confused with many other clinically aggressive disorders,

precision in diagnosis is essential both to proper clinical management and subsequent genetic counselling. Hence, this study was taken up in order to diagnose these conditions and administer suitable counselling measures to minimise the incidence of sickle cell disease in the future. Aim: The aim of this study was to identify the spectrum of all Sickle cell diseases diagnosed at a tertiary care centre in Bangalore, Karnataka, India who presented over a period of five years from 2009 to 2013 and also to screen the parents and siblings of the patients for their carrier status. Materials and Methods: We reviewed 26 cases of Sickle Cell Disease (SCD) and also 38 parents & 10 siblings of these children for their carrier status. Haemoglobin electrophoreses was performed by using alkaline gel method, followed by High Performance Liquid Chromatography when needed. Results: A total of 26 children diagnosed with SCD were enrolled in the study. Most common entity was Sickle Cell Anaemia (SCA), followed by sickle thalassaemia and Sickle Cell Trait (SCT). Commonest clinical presentation was fever and pallor. Amongst the parents and siblings, sickle cell trait was the most common entity followed by thalassaemia trait. One interesting case of HbSE disease was encountered, which is a rare entity in India. Conclusion: This study brings out the total spectrum of SCDs in a tertiary care centre in Karnataka, with more emphasis on screening of the parents and siblings for their carrier status.

190. Effectiveness and Feasibility of Weekly Iron and Folic Acid Supplementation to Adolescent Girls and Boys through Peer Educators at Community Level in the Tribal Area of Gujarat.

2016

Indian Journal of Community Medicine

Shah, Shobha P and Shah, Pankaj and Desai, Shrey and Modi, Dhiren and Desai, Gaytri and Arora, Honey

Background: Anemia during adolescence affects growth and development of girls and boys increasing their vulnerability to dropping out-of-school. Hence investing in preventing anemia during adolescence is critical for their survival, growth and development. Objective: To find out the burden of anemia on adolescent age group in the tribal area of Jhagadia block and to assess the change in the hemoglobin level through the weekly Iron and Folic Acid IFA (DOTS) directly observed treatment supplementation under Supervision by Peer Educators at Community level among adolescents. Methods: Community based intervention study conducted with adolescents (117 girls and 127 boys) aged 10-19 years, through supplementation of IFA (DOTS) by trained Peer Educators for 52 weeks in 5 tribal villages of Jhagadia. Hemoglobin level was determined by HemoCue method before and after intervention and sickle cell anemia by Electrophoresis method. Primary data on hemoglobin and number of tablets consumed was collected and statistically analyzed in SPSS 16.0 software by applying paired t-test. Results: The overall findings suggest that the prevalence of anemia reduced from 79.5% to 58% among adolescent girls and from 64% to 39% among boys. Mean rise of hemoglobin seen was 1.5 g/dl among adolescent boys and 1.3 g/dl among girls. A significant association was found in change in hemoglobin before and after intervention (P = 0.000) Conclusion: Prevalence of anemia among girls and boys can be reduced in their adolescent phase of life, through weekly supplementation of iron folic acid tablets under direct supervision and Nutrition Education by Peer Educator at community level.

191. Prevalence of thalassemia and hemoglobinopathy in eastern India: A 10-year high-performance liquid chromatography study of 119,336 cases.

2016

Asian Journal of Transfusion Science

Mondal, Santosh Kumar and Mandal, Saikat

Background: Hereditary hemoglobin (Hb) disorders are the most commonly encountered single gene disorders in India. Proper timely identification of these disorders is of paramount importance to prevent thalassemia major and clinically severe hemoglobinopathy as well as for epidemiologic purposes. Aims: Our aim was to determine the prevalence of thalassemia and hemoglobinopathy in patients of a tertiary care hospital of West Bengal, India. Materials and Methods: This prospective study was conducted on 119,336 cases over a period of 10 years. After

taking clinical history and familial history, complete hemogram report was obtained by an automated cell counter. High-performance liquid chromatography (HPLC) was performed on the samples with Bio-Rad Variant using beta thalassemia short program. Confirmatory tests were performed whenever required. Results: A normal Hb pattern was observed in 104,804 (87.83%) cases and abnormalities were detected in 14,532 (12.17%) patients. Î² (beta) thalassemia trait was the commonest abnormality found in 5,488 (4.60%) patients. HbE trait was found in 3,604 (3.02%) patients, Î² thalassemia major/intermedia in 1,981 (1.66%) cases, and EÎ² thalassemia in 1,384 (1.16 %) cases. Other variants detected included HbE disease, sickle-cell disease, sickle Î² thalassemia, HbD-Punjab trait, HbQ-India trait, Î±-thal trait, double heterozygous state of HbS and HbE, double heterozygous state of HbS and HbD, HbJ-Meerut, hereditary persistence of fetal hemoglobin (HPFH), HbH, delta Î²-thal trait, and Hb Lepore. Conclusion: In view of the high prevalence of hemoglobinopathy in this region, a routine premarital screening program is needed for the identification and prevention of high-risk marriages and thus, prevention of the psychosocial trauma of bearing a transfusion-dependent child for life.

192. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates.

2013

Lancet

FB, Piel and AP, Patil and RE, Howes and OA, Nyangiri and PW, Gething and Dewi, M and WH, Temperley and TN, Williams and DJ, Weatherall and SI, Hay and Piel, FrÃ©dÃ©ric B and Patil, Anand P and Howes, Rosalind E and Nyangiri, Oscar A and Gething, Peter W and Dewi, Mewahyu and Temperley, William H and Williams, Thomas N and Weatherall, David J and Hay, Simon I

Background: Reliable estimates of populations affected by diseases are necessary to guide efficient allocation of public health resources. Sickle haemoglobin (HbS) is the most common and clinically significant haemoglobin structural variant, but no contemporary estimates exist of the global populations affected. Moreover, the precision of available national estimates of heterozygous (AS) and homozygous (SS) neonates is unknown. We aimed to provide evidence-based estimates at various scales, with uncertainty measures.Methods: Using a database of sickle haemoglobin surveys, we created a contemporary global map of HbS allele frequency distribution within a Bayesian geostatistical model. The pairing of this map with demographic data enabled calculation of global, regional, and national estimates of the annual number of AS and SS neonates. Subnational estimates were also calculated in data-rich areas.Findings: Our map shows subnational spatial heterogeneities and high allele frequencies across most of sub-Saharan Africa, the Middle East, and India, as well as gene flow following migrations to western Europe and the eastern coast of the Americas. Accounting for local heterogeneities and demographic factors, we estimated that the global number of neonates affected by HbS in 2010 included 5,476,000 (IQR 5,291,000-5,679,000) AS neonates and 312,000 (294,000-330,000) SS neonates. These global estimates are higher than previous conservative estimates. Important differences predicted at the national level are discussed.Interpretation: HbS will have an increasing effect on public health systems. Our estimates can help countries and the international community gauge the need for appropriate diagnoses and genetic counselling to reduce the number of neonates affected. Similar mapping and modelling methods could be used for other inherited disorders.Funding: The Wellcome Trust.

193. Prevalence of Sickle Cell Disease Among School-age Children in Chhattisgarh, India: Predictions, Implications and Interventions.

2019

Journal of Health Management

Mishra, H and Neralwar, A

Sickle cell disease (SCD) is a haemoglobin disorder prevalent in Sub-Saharan Africa, Middle East and India. SCD is a major cause of morbidity and low quality of life in Chhattisgarh and other central Indian states. Currently, there is no estimate available for the number of SCD patients and carriers in Chhattisgarh. The Government of Chhattisgarh conducted a screening project for measuring prevalence of SCD among school-age children in the state in October 2007â€“December 2017 in six districts of the state. Using these screening data, an estimate of prevalence of SCD was made for school-age children in different geographical regions and social categories in Chhattisgarh. The numbers of SCD patients and carriers among school-age children in Chhattisgarh were estimated as 27,101 and 714,483, respectively. Furthermore, 79.64 per cent patients among school-age children, that is, 21,583 patients were estimated to reside in rural areas. The estimates may be of use in designing policies and developing strategies with better coordination and outreach for care of SCD patients. It is call of the time to develop dedicated infrastructure having medical, training, counselling and research facilities in a hierarchical manner comprising dedicated tertiary to primary care facilities in remote rural areas.

194.Sickle cell disease in India.

2002

Current Opinion in Hematology

Mohanty, Dipika and Mukherjee, Malay B

The clinical manifestations of sickle cell anemia in India seem to be milder than in Africa and Jamaica. Mostly homozygous sickle cell anemia patients seek treatment for vaso-occlusive crises, which have greatest incidence during the rainy season, followed by winter. It is interesting to note that both sickle cell anemia patients and carriers (heterozygotes) have iron deficiency. alpha Thalassemia is one of the major epistatic factors responsible for amelioration of the disease. Simple measures like vaccination in childhood, adequate oral intake of fluids with electrolytes during vaso-occlusive crises, and avoidance of exposure to extreme temperatures reduce the number of patients with vaso-occlusive crises. Premarital counseling and prenatal diagnosis also help reduce the number of births of homozygous children.

195.Hemoglobin disorders in South India.

2011

ISRN Hematology

Chandrashekar, V and Soni, M

Cation exchange-high performance liquid chromatography (CE-HPLC) is increasingly being used as a first line of investigation for hemoglobinopathies and thalassemias. Together with a complete blood count, the CE-HPLC is effective in categorizing hemoglobinopathies as traits, homozygous disorders and compound heterozygous disorders. We carried out a one year study in Apollo Hospitals, Chennai (Tamil Nadu, South India) during which 543 abnormal chromatogram patterns were seen. The commonest disorder we encountered was Î²-thalassemia trait (37.9%), followed by HbE trait (23.2%), homozygous HbE disease (18.9%), HbS trait (5.3%), HbE Î²-thalassemia (4.6%), HbS Î²-thalassemia (2.5%), Î²-thalassemia major (2.3%), HbH (1.6%), homozygous HbS (1.4%), HbD trait (0.7%). The average value of HbA2 in Î²-thalassemia minor was 5.4%. Î²-thalassemia major had an average HbF of 88% and in HbH the mean A2 was 1.4%. Among the HbE disorders the HbA2 + HbE was 30.1% in the heterozygous state, 90.8% in the homozygous state and 54.8% in HbE Î²-thalassemia. In the sickle cell disorders, HbS varied from 30.9% in the trait to 79.9% in the homozygous state to 65.6% in HbS Î²-thalassemia.

196.Global epidemiology of haemoglobin disorders and derived service indicators.

2008

Bulletin of the World Health Organization

Modell, B and Darlison, M

To demonstrate a method for using genetic epidemiological data to assess the needs for equitable and cost-effective services for the treatment and prevention of haemoglobin disorders. We obtained data on demographics and prevalence of gene variants responsible for haemoglobin disorders from online databases, reference resources, and published articles. A global epidemiological database for haemoglobin disorders by country was established, including five practical service indicators to express the needs for care (indicator 1) and prevention (indicators 2-5). Haemoglobin disorders present a significant health problem in 71% of 229 countries, and these 71% of countries include 89% of all births worldwide. Over 330,000 affected infants are born annually (83% sickle cell disorders, 17% thalassaemias). Haemoglobin disorders account for about 3.4% of deaths in children less than 5 years of age. Globally, around 7% of pregnant women carry b or a zero thalassaemia, or haemoglobin S, C, D Punjab or E, and over 1% of couples are at risk. Carriers and at-risk couples should be informed of their risk and the options for reducing it. Screening for haemoglobin disorders should form part of basic health services in most countries.

197. Sickle cell disease and pregnancy outcomes: a study of the community-based hospital in a tribal block of Gujarat, India.

2017

Journal of Health, Population & Nutrition

Desai, Gayatri and Anand, Ankit and Shah, Pankaj and Shah, Shobha and Dave, Kapilkumar and Bhatt, Hardik and Desai, Shrey and Modi, Dhiren

Background: Sickle cell disease (SCD) is a hereditary blood disorder prevalent in tribal regions of India. SCD can increase complications during pregnancy and in turn negatively influence pregnancy outcomes. This study reports the analysis of tribal maternal admissions in the community-based hospital of SEWA Rural (Kasturba Maternity Hospital) in Jhagadia block, Gujarat. The objective of the study is to compare the pregnancy outcomes among SCD, sickle cell trait and non-SCD admissions. This study also estimated the risk of adverse pregnancy outcomes for SCD admissions.Methods: The data pertains to four and half years from March 2011 to September 2015. The total tribal maternal admissions were 14640, out of which 10519 admissions were deliveries. The admissions were classified as sickle cell disease, sickle cell trait and non-sickle cell disease. The selected pregnancy outcomes and maternal complications were abortion, stillbirth, Caesarean section, haemoglobin levels, blood transfusion, preterm pregnancy, newborn birth weight and other diagnosed morbidities (IUGR, PIH, eclampsia, preterm labour pain). The odds ratios for each risk factor were estimated for sickle cell patients. The odds ratios were adjusted for the respective years.Results: Overall, 1.2% (131 out of 10519) of tribal delivery admissions was sickle cell admissions. Another 15.6% (1645 out of 10519) of tribal delivery admissions have sickle cell trait. The percentage of stillbirth was 9.9% among sickle cell delivery admission compared to 4.2% among non-sickle cell deliveries admissions. Among sickle cell deliveries, 70.2% were low birth weight compared to 43.8% of non-sickle cell patient. Similarly, almost half of the sickle cell deliveries needed the blood transfusion. The 45.0% of sickle cell delivery admissions were pre-term births, compared to 17.3% in non-SCD deliveries. The odds ratio of severe anaemia, stillbirth, blood transfusion, Caesarean section, and low birth weight was significantly higher for sickle cell admissions compared to non-sickle cell admissions.Conclusions: The study exhibited that there is a high risk of adverse pregnancy outcomes for women with SCD. It may also be associated with the poor maternal and neonatal health in these tribal regions. Thus, the study advocates the need for better management of SCD in tribal Gujarat.

198. Sickle Cell Disease in Central India: A Potentially Severe Syndrome.

2016

Indian Journal of Pediatrics

Jain, Dipty and Warthe, Vinit and Dayama, Paridhi and Sarate, Dilip and Colah, Roshan and Mehta, Pallavi and Serjeant, Graham

Objectives: To explore clinical, hematological and molecular features of homozygous sickle cell (SS) disease in central India.Methods: Focusing on the pediatric age group attending a clinic at the Akola Government Medical College, Akola, Maharashtra State, India, a cross-sectional assessment of 91 patients with sickle cell disease was performed during one week in March 2015.Results: Of the 91 patients, there were 49 with SS disease, 36 with sickle cell-beta thalassemia, and 6 with sickle cell-HbD Punjab. Alpha globin gene deletions occurred in only 8/49 (16Â %) SS disease but fetal hemoglobin (HbF) levels were markedly elevated with mean and median of 24.4Â %; all except 3 SS disease patients had the Xmn1(+/+) polymorphism consistent with the Asian haplotype. Among the 36 patients with sickle cell-beta thalassemia, 25 (69Â %) had the severe beta(+) mutation, IVS1-5Â GÂ >Â C, and seven other molecular mutations, all beta(o) occurred in the other 11 patients. Many patients had a relatively severe clinical course. Comparison of SS disease and sickle cell-beta thalassemia showed no differences in the prevalence of dactylitis, bone pain crisis, acute chest syndrome, hemoglobin level, reticulocyte counts or hydroxyurea usage but patients with sickle cell-beta thalassemia had significantly more blood transfusions, and greater frequencies of splenomegaly and hepatomegaly.Conclusions: Many patients in central India have relatively severe manifestations. This may result from lower frequencies of alpha thalassemia and more frequent severe sickle cell-beta(+) thalassemia. There is a need for assessment of the indications and policies for blood transfusion and for hydroxyurea.

199. Prevalence of globin gene modifiers encountered in fetuses during antenatal diagnosis of hemoglobinopathies.

2020

International Journal of Laboratory Hematology

Mehta, Pallavi and Sawant, Pratibha and Gorivale, Manju and Nadkarni, Anita and Colah, Roshan and Mukherjee, Malay B

Introduction: The hemoglobinopathies are the commonest group of single gene disorders in the Indian subcontinent. Although genetic modifiers are known to have a remarkable effect on phenotypic expression, the effects of the possible coâ€inheritance of different modifiers are not taken into account during prenatal diagnosis. The present study was undertaken to look for the frequency of globin gene modifiers like the types of Î²â€globin gene mutations, Î± thalassemia, Î± gene triplication, and the Xmn1 polymorphism in fetuses during antenatal diagnosis of hemoglobinopathies. Materials and methods: A total of 580 fetuses with different diagnoses were screened for the presence of genetic modifiers. Results: Twentyâ€two different Î²â€globin gene mutations were identified of which 3.5% were milder mutations. Among the affected fetuses, 29.6% of the Î²â€thalassemia major and 52.9% of the sickle cell anemia (SCA) fetuses had one genetic modifier while 3.7% of the Î²â€thalassemia major and 41.1% of the SCA fetuses had coâ€inherited two modifiers. Î±â€gene triplication was detected in 16 (3.5%) Î²â€thalassemia/sickle cell heterozygous and normal fetuses of which 5 babies (2 Î²â€thalassemia heterozygous and 3 normal) could be followed up. Of the 2 Î²â€thalassemia heterozygous babies, one had a severe clinical presentation. Conclusion: Many fetuses had one or two gene modifiers. However, the impact of these on ameliorating the severity of the disease could not be evaluated as all the fetuses with Î² thalassemia major or sickle cell disease were terminated. Parents having heterozygous fetuses with Î± gene triplication should be followed up periodically after birth for better management of these babies.

200. Prevalence of Deletional Alpha Thalassemia and Sickle Gene in a Tribal Dominated Malaria Endemic Area of Eastern India.

2014

ISRN Hematology

Purohit, Prasanta and Dehury, Snehadhini and Patel, Siris and Patel, Dilip Kumar

Inherited hemoglobin disorders like alpha thalassemia and sickle gene are common in the Indian subcontinent. These disorders in the heterozygous state act as malaria resistance genes and influence the susceptibility to

Plasmodium falciparum malaria. There is inadequate knowledge about the epidemiology of these malaria resistance genes in the tribal dominated malaria endemic region of the state of Odisha in eastern India. A cross sectional prevalence study was undertaken in 594 subjects in five tribal populations in this region, namely, Sahara (42.4%), Kutia Kandha (30.0%), Kuda (15.8%), Gond (9.8%), and Oraon (2.0%). Sickling test, Hb electrophoresis, HPLC, and molecular studies were undertaken to diagnose the prevalence of sickle allele, Î²-thalassemia allele, and deletional alpha thalassemia. Sickle and Î² thalassemia alleles were found in 13.1% and 3.4% of subjects, respectively. Sickle allele was found both in heterozygous (10.1%) and homozygous state (3.03%). The prevalence of alpha thalassemia was 50.84% with an allelic frequency of 0.37. Both Î±-3,7 and Î±-4,2 alpha thalassemia were detected with an allele frequency of 0.33 and 0.04, respectively. The high prevalence of alpha thalassemia and sickle gene in this population is probably due to selection pressure of endemic malaria in this part of India.

201. Bacteraemia in children with sickle cell disease: Indian scenario

2009

American Journal of Hematology

Jain, D and Chandak, A and Deopujari, S

Background: Bacteraemia frequently complicates the course of sickle cell disease. Mortality due to infections is higher in patients with sickle cell disease. Objective: Despite a high incidence of infection in children with sickle cell disease, studies regarding the causes of Bacteraemia in India are few. Hence this study was carried out with the purpose of identifying the causative organism in children with sickle cell disease with infections. Method: A hospital based, cross sectional study was undertaken in tertiary care hospital. Children with homozygous sickle cell disease <18 yrs of age with axillary temp> 38.5 were included in study. Results: Of the 368 children enrolled in the study, 94 had a positive blood culture. Gram positive organisms were responsible for 67% of Bacteraemia and gram negative 33% of cases. The dominant organism was Staphylococcus aureus in 60% and Salmonella in 18%. Streptococcus pneumoniae was the cause of infection in only 1% of children. Staphylococcus aureus was responsible for 50% of the total mortality due to infections. Acute painful crisis was the most co-morbidity associated with bacteraemia (60%) Conclusion: There seems to be a different spectrum of organisms causing infection in patients with sickle cell disease in developed and the developing world. The study indicates majority 60% of the infections due to Staphylococcus aureus and 18 % due to Salmonella, in contrast to the developed world, where maximum infections are due to Streptococcus pneumoniae. The study thus raises the question of justification of the pneumococcal prophylaxis in developing world.

202. Extrapolation Pitfalls and Methodology Flaws in Curing Anemia via Parental Education and Counseling - Reply

2020

JAMA Pediatrics

Zhou MD, Bo and Niu PhD, Wenquan and Shet MD, PhD, Arun S and Zwarenstein MD, PhD, Merrick and Galanti MD, PhD, Maria Rosaria and Shet, A S and Zwarenstein, M and Galanti, M R and Zhou MD, Bo and Niu PhD, Wenquan and Shet MD, PhD, Arun S and Zwarenstein MD, PhD, Merrick and Galanti MD, PhD, Maria Rosaria

Shet et al respond to a critique of their study on curing anemia via parental education and counseling by Zhou and Niu. The authors raise 2 specific issues that they believe are legitimate. First, Zhou and Niu question the generalizability of the trial conducted in Chamarajnagar district, South India, to rural children from the rest of India. In support of their concern is cited evidence for genetic diversity among Indian individuals and documentation of rare germline mutations in TMPRSS6, which encodes a type II transmembrane serine protease produced by the liver that regulates the expression of the systemic iron regulatory hormone hepcidin that can cause iron-refractory iron-deficiency anemia.

203. Detection of hemoglobinopathies and thalassaemia in Delhi Punjab and Haryana using CE-HPLC: Study on 8240 subjects

2016

Indian Journal of Clinical Biochemistry

Kuchhal, N K and Aggarwal, S and Jha, V

Introduction and Background: Hereditary disorders of Hb mainly includes hemoglobinopathies and thalassaemia. Early and accurate detection of these disorders are immensely important both epidemiology and economically. These disorders can be prevented simply by population screening using Cation exchange High performance liquid chromatography (CE-HPLC), a technique introduced for the accurate and quick screening of hemoglobinopathies and thalassaemias. Worldwide, approximately 250 million people constituting 4.5 % of the world population carry beta thalassemic gene and in India alone, the number is approximately 30 million with 50 % in South East Asia. Similarly the burden of hemoglobinopathies in India is high with nearly 12,000 infants being born every year with severe disorders. These numbers imply that every hour 1 child is born, who may suffer with this genetic disorder. The present study was undertaken to evaluate the spectrum and frequency of various hemoglobinopathies and thalassaemia in the main city Delhi and adjoining states of Haryana and Punjab from where we have been receiving the maximum number of blood samples for Hemoglobinopathies screening. Patient/Material and Methods: The present single centre (Bio Diagnostics, Rohini), retrospective cross-sectional study was carried out on 8240 subjects which included 7860 antenatal mothers and 380 males The Study centre is a private lab specialized in doing Immuno-Assays, HPLC and Molecular Biology since 1991 in Delhi at Rohini. The lab is approved by BARC for doing RIA. The whole blood samples were received in K3 EDTA vacutainers and were analysed on the same day in a batch of 10-20 sample after receiving. CBC's were done on KX-21, Sysmex corporation and HPLC were done on D1O Bio-Rad fully automated Analyzer. The period of study was from April 2013 to Feb 2016. Patients with a recent history of blood transfusion were excluded from this study. Results and Discussion: Out of 8240 subjects were screened during the period of approximately three years, of which 7860 (95.5 %) were antenatal mothers and 380 (4.5 %) males. Almost all the subjects were Hindu. Overall 7560 were normal (91.74 %), while 680 (8.26 %) were abnormal of which 640 (7.77 %) were females and 40 (0.49 %) were males. Among the abnormal cases we have detected, 440 cases (400 female and 40 male) (5.33 %) of beta thalassemia minor (BTT), 90 cases of HbD Punjab (1.09 %) and 34 cases (0.48 %) of Hb E heterozygous 32 (0.38 %) cases of Hb J Meerut, 12 (0.14 %) case of Hb Q India and 4 case (0.04 %) of HbD Iran 8 cases of beta thalassaemia major (0.09 %), 11 cases of sickle cell disease (0.13 %) 24 cases of double heterozygous of beta thal with sickle (0.29 %) and 25 cases HbE with beta thal (0.30 %). CE-HPLC is a sensitive quick and accurate method for screening hemoglobinopathies. Conclusion: The study indicates that there is high prevalence of BTT and HbD Punjab in the state of Delhi, Punjab and Haryana.

204. Prevalence of sickle cell disorder and anaemia in tribal school students from central India

2012

International Journal of Collaborative Research on Internal Medicine and Public Health

Gunjal, S S and Narlawar, U W and Humne, A Y and Chaudhari, V L and Gunjal Sandeep, S and Narlawar Uday, W and Humne Arun, Y and Chaudhari Vijaya, V L and Gunjal, S S and Narlawar, U W and Humne, A Y and Chaudhari, V L

Background: Tribal health is matter of concern in India. The problem of anaemia is very rampant in this population. All the health problem in tribals are complicated by presence of Sickle Cell Disorders which has a presence in tribal communities of Central India. These problems are severe in tribal children. So this study was undertaken in Residential Tribal schools. Objectives: (1) To find prevalence of Sickle Cell Disorders in Residential Tribal School students (2) To find the prevalence of anaemia in them (3) To study their nutritional status with reference to above findings Material and Methods: The study was conducted in July-August 2009 in 908 students studying in two different Residential Tribal Schools in Central India. Every individual was screened

for Sickle Cell Disorder by performing solubility test on finger prick sample of blood. Those subjects found positive on screening were subjected to Hb electrophoresis. Hb estimation was done by Cynmethaemoglobin method. Other information was recorded on pretested pro forma by trained investigators. Data was analyzed by appropriate statistical methods. Results: Sickle Cell Disorder was present in 6.28% of study subjects. (7.99% in boys and 2.20% in girls) Prevalence of anaemia was 89.75%. (28.31% mild, 29.40% moderate, 32.04% severe anaemia) In boys, 87.69% students were anaemic while in girls 91.91% students were anaemic. All subjects with sickle cell disorder were anaemic. Conclusions: Sickle Cell disorders has wide spread presence in different tribes of Central India. Problem of anaemia is long lasting and severe and is more in case of girls.

205.Iron deficiency anaemia in sickle cell disorders in India

2008

Indian Journal of Medical Research

Mohanty, D and Mukherjee, M B and Colah, R B and Wadia, M and Ghosh, K and Chottray, G P and Jain, D and Italia, Y and Ashokan, K and Kaul, R and Shukla, D K and Muthuswamy, V and Mohanty D, Mukherjee M B Colah R B Wadia M Ghosh K Chottray G P Jain D Italia Y Ashokan K Kaul R Shukla D K and Muthuswamy, V

Background & objectives: Iron deficiency anaemia (IDA) is uncommon in individuals with sickle cell diseasc (SCD) because of availability of an adequate iron source potentially from increased red cell turnover and from blood transfusions. Also, iron deficiency anaemia can often go unnoticed because the sickle cell disease patients are already anaemic. Iron deficiency in sickle cell patients may result in lowering the intracellular haemoglobin concentration and this may ameliorate sickling. The present study was undertaken to determine the prevalence of iron deficiency anaemia and the response of iron supplementation in sickle cell disorders in tribal population of the four States viz. Maharashtra, Gujarat, Orissa and Tamil Nadu. Methods: A total of 8434 individuals (7105 AA, 1267 AS and 62 SS) were tesled for zinc protoporphyrin/haem (ZPP/H) ratio and haemoglobin levels. Twenty two sickle cell anaemia (SS), 47 sickle cell trait (AS) and 150 normal control (AA) individuals who were iron deficient, were given iron therapy for a period of 12 wk and the laboratory investigations were repeated at the 13th wk. Results: Sixty seven per cent of subjects with sickle cell anaemia and 26 per cent with sickle cell trait had elevated ZPP/H ratios (>80 Î¼mol/mol) as against 22.8 per cent of normal individuals. The elevated ZPP/H ratios is an indicator of microcytic anaemia of iron deficiency. Following iron therapy, an improvement in the Hb levels and ZPP/H ratios was observed in both sickle cell disorders and normal individual cases. Interpretation & conclusions: This study suggests that iron deficiency anaemia is an important problem in Indian sickle cell anaemia patients and iron supplementation should be given only in proven cases of iron deficiency anaemia.

206.Sickle cell trait and disease among tribal communities in Orissa, Madhya Pradesh and Kerala

1997

Indian Journal of Medical Research

Kaur, M and Das, G P and Verma, I C and Kaur M, Das G P and Verma, I C and Kaur, M and Das, G P and Verma, I C

A study of 2570 tribals comprising 973 from Kerala, 696 from Madhya Pradesh and 901 from Orissa revealed the frequency of sickle cell gene to vary from 0.05 to 0.31 among different communities. High frequency of the gene (0.145 or more) was observed among Chettys, Kurmars and Kondhs, who also had a substantial number of homozygous sicklers. None of those with sickle cell disease (HbSS) were more than 39 yr in age as compared with 9.9-35.3 per cent among heterozygotes (HbAS). Mean foetal haemoglobin in those with sickle cell disease varied between 9.7 to 13.5 per cent, although it showed a slight positive correlation with total haemoglobin only among the Kondhs. Painful crises were universally observed among all tribals with sickle cell disease, with jaundice being present in 57.5 per cent of cases. Some carriers of sickle cell gene also complained of painful

crises. A health plan for identifying homozygotes in infancy with appropriate medical management is highly desirable.

207. Erratum: Determination of toral antioxidant capacity of saliva in sickle cell anemic patients - A cross-sectional study

2017

Journal of the Indian Society of Pedodontics and Preventive Dentistry

Baliga, Sudhindra and Chaudhary, Minal and Bhat, Sham and Bhatiya, Poonam and Thosar, Nilima and Bhansali, Pooja

Background: Sickle cell anemia is a congenital hemoglobinopathy characterized by deformed red blood cells. Oxidative stress plays an important role in the pathophysiology of sickle cell anaemia as it destroys free radicals, and thereby depleting the protective mechanisms such as antioxidants in serum. These antioxidants are essential to protect against harmful oxidation-reduction reactions preventing oxidative damage to the cells. Aim: To evaluate and compare the Total Antioxidant Capacity (TAC) of serum and saliva in sickle cell anemia patients. Materials and Methods: A total of 150 children aged 4-12 yrs were selected and divided into two equal groups: Children suffering from sickle cell anemia and healthy controls. Blood and saliva samples were collected aseptically from both groups and were subjected to phosphomolybdenum method. Absorbance was read spectrophotometrically at 695 nm. The concentration of total antioxidants was obtained by plotting absorbance of the test against the standard graph. Results: TAC levels in serum (0.29+-0.19) and saliva (0.29+-0.14) of sickle cell anaemic patients was reduced when compared with serum (0.32+ 0.18) and saliva (0.33+ 0.16) of the healthy children. The correlation between levels of TAC in saliva and serum was found to be statistically significant in sickle cell anaemic patients. Conclusion: A significant correlation of the TAC was found in saliva and serum of the patients with SCA suggests that saliva could be used as a non invasive alternative for assessing the antioxidant status in patients with SCA.

208. Haemoglobinopathies in eastern Indian states: a demographic evaluation

2014

Journal of Community Genetics

Nagar, Rachana and Sinha, Sujata and Raman, Rajiva

Haemoglobinopathies are a leading cause of child mortality worldwide, although with a variable geographical incidence. A reliable estimate of prevalence of the disease is necessary for reducing its burden. However, most studies in India are either hospital based or from certain regions of the country and hence may not realistically reflect the disease burden. The eastern Indian states of Bihar, Chhattisgarh and Jharkhand and eastern region of Uttar Pradesh, which comprise ~25Â % population of the country, are poorly studied with respect to haemoglobinopathies. The present study, conducted on 1,642 individuals from this region, shows a frequency of 3.4Â % for Î²-thalassaemia trait (BTT), 3.4Â % for sickle cell haemoglobin trait (HbS)/haemoglobin E trait (HbE) and 18Â % for Î±-globin defects. While BTT mutations are distributed rather uniformly across the region, HbS occurs only in Chhattisgarh and Jharkhand, the regions rich in tribal populations. The frequency of Î±-gene mutation is strikingly high, occurring even in individuals with normal blood count, in tribal as well as non-tribal groups. The mutation spectrum of BTT is also distinct since the common mutations, IVS1-1 (G-T) and 619Â bp del, are absent while CD15 (G-A) is the second most frequent. The HbA2 level in the suspected cases is strikingly low. We demonstrate association of the low HbA2 level with vitamin B12 and folate deficiency in this cohort. Thus, the present report besides providing an estimate of the carrier frequency of Î²-thalassaemia traits also confirms high prevalence of Î±-gene defects and regional heterogeneity in distribution of HbS in the eastern parts of India.

209. The Screening and Morbidity Pattern of Sickle Cell Anemia in Chhattisgarh

2014

Indian Journal of Hematology and Blood Transfusion

Panigrahi, Sumanta and Patra, P K and Khodiar, P K

Our objective was to find out prevalence of sickle cell anemia among the population of three districts (Kanker, Dantewada and Raigarh) of Chhattisgarh with clinical and hematological profile of sickle cell disease patients. A cross sectional study was done. A total of 15,701 persons collectively from three districts voluntarily attended the mobile camp and were screened for sickle cell anemia. First solubility test were done and were confirmed by Hb electrophoresis. The prevalence of sickle cell trait (HbAS) was 1,672 (10.6Â %), sickle cell disease (HbSS) and inconclusive band was 97 (0.66Â %). The HbSS and inconclusive band were subjected to HPLC. Among them 12 (0.076Â %) cases were double heterozygous for Hb-S and beta thalassemia minor (SB+), 2 (0.012Â %) cases were double heterozygous for Hb-S and Hb-E (S/HBE), 1 (0.006Â %) case was double heterozygous for Hb-S and Hb-D Punjab (S/HBD) and 22 (0.14Â %) cases had Hb-S with Hb-F level more than 20Â % (SSF). Maximum number of HbSS cases were 13 (2.29Â %) out of 567 children in the age group 0â€“5Â years and HbAS cases were 124 (15.6Â %) out of 794 persons in the age group 21â€“25Â years. On comparison between vaso-occlusive and steady state, homozygous patients showed decrease in Hb, HCT, MCH, RBC in vaso-occlusive crises (pÂ <Â 0.001) than steady state. Also there was one moderate negative correlation in number of blood transfusion (rÂ =Â 0.46) with fetal hemoglobin (HbF) level. Patients with high HbF can have severe disease. This happens due to uneven distribution of fetal hemoglobin in F-cells with mean HbF remaining constant but in our study, those who had HbF level above 15â€“20Â % were having fewer crises.

210. Sickle cell anaemia-community control program for tribal population groups of satpuda hilly ranges from nandurbar, dist maharashtra

2014

Indian Journal of Human Genetics

Prabhune, Y S and Dalvi, P N and Kulkarni, G T and Kate, S L

During last 10 years of 20th Century we screened most of the tribal population groups from state of Maharashtra and found that Madia, Pardhan, Otkar and other tribal groups from Gadchiroli Dist. and Bhill and Pawara tribal population groups from Nandurbar District have higher prevalence of sickle cell disorder. (Heterozygous >20%). We identified three voluntary health organization i.e. SEARCH of Dr. Abhay Bang, LOKBIRADARI project of Dr. Prakash Amte and AMHI AMCHYA AROGYASATHI of Dr. Satish Gogulwar, trained their staff members and encourage them to undertake work on Sickle Cell Anaemia. There was no any NGO working on this problem from Nandurbar District, hence in 1998 Maharashtra Arogya Mandal established Community Control Program Centre in Satpuda hilly ranges (Nandurbar district) with help of local tribal youths. The centre is popularly known as Sickle Cell Dawakhana (Roshmal Budurk, Taluka Dhadgaon, Dist. Nandurbar.) We provide all the following facilities â€¢ Accurate diagnosis â€¢ Possible Treatment and follow up â€¢ Population genetic surveys â€¢ Health education â€¢ Improvement in the quality of life (QOL) â€¢ Genetic counselling â€¢ Marriage counselling â€¢ Prenatal diagnosis â€¢ Research â€¢ Training We are working in this area for last sixteen years. We screened more than 1.5 lakhs tribal people and more than 2000 patients are under our medical supervision. Patients and parents are happy with our medical treatment and we have good response. Our ten point programme will be presented.

211.Stem cell banking: Are South Indian mothers aware?

2018

Cell and Tissue Banking

Rajendran, Sharun and Kirubhakaran, Arthi and Alaudheen, Rakshana and Jayaramayya, Kaavya and Santhanakalai, Mahalakshmi and Jayaraman, Sanjeevagandhan and Chinnaraju, Sukumar and Reddy, Janardhana Kumar and Vellingiri, Balachandar

Umbilical cord blood (UCB) is an important source of stem cells, the heart of regenerative medicine. As the globalization and population of the world continues to increase, we are faced with an inundation of new diseases, affecting millions of people. Research work considering stem cells is essential for developing therapy for various conditions. Reduced availability of UCB serves as a hindrance to promote further research. Hence, India being one of the most densely populated countries in the world, can be considered a potential UCB repository. In this study 428 mothers of children born in the period from 2012 to 2017 were asked to fill questionnaires that evaluated their awareness regarding stem cell banking. This investigation deliberates if expectant mothers in this region are aware of stem cell banking and if there is a significant pattern regarding awareness based on parameters like age, educational qualification, locality, annual income and consulted hospitals. Although, majority of the women were unaware of this facility, knowledge was heightened in wealthy, educated, women from urban areas who consulted private hospitals. Hence, great efforts need to be made to further the awareness of expectant mothers in South India regarding UCB storage and donation.

212.Allogeneic Stem Cell Transplantation In Children: Single Centre Experience From North India

2018

Pediatric Hematology Oncology Journal

Vyas, C and Sachdev, M and Pandit, A and Dua, V

BACKGROUND: Allogeneic stem cell transplant (allo-SCT) services in children are still far behind in India as compared to the developed countries because of the resource constraints. We present our experience of allo-SCT for various benign and malignant paediatric diseases. METHODS: A retrospective analysis of children who underwent allo-SCT between January 2014 and May 2018 at our centre was done. The indications for allo-SCT were hemoglobinopathy [thalassemia major(TM)-27, sickle cell disease(SCD)-12], aplastic anemia-23, Fanconi anaemia-13, Diamond-Blackfan anemia-2, immunodeficiency (mucopolysaacharidoisis-2, Wiskott-Aldrich syndrome-2 and Chediak-Higashi syndrome-1), acute myeloid leukaemia (AML)-12, acute lymphoblastic leukaemia (ALL)-21, juvenile myelomonocytic leukaemia (JMML)-2, myelodysplastic syndrome-2, relapse neuroblastoma-1 and chronic myeloid leukaemia (CML)-4. Donors were HLA-matched sibling-66, haploidentical-32, single antigen mismatch-7 and matched unrelated-19. The source of stem cells was peripheral blood in 108 patients and bone marrow in 16 patients. We chose a post-transplant cyclophosphamide based approach in majority of haploidentical transplants. RESULTS: A total of 124 patients (75 male and 49 female) with a mean age of 9 years (range, 14 monthsâ€“18 years) underwent allo-SCT. The median time for neutrophil engraftment was 13 days (range, 11- 18 days). Ten patients (8%) had rejection (TM-4, SCD-1, AML-1, ALL-1, immunodeficiency-1, Fanconi-1 and JMML-1). Acute graft versus host disease (GVHD) was reported in 31% patients (grade III/IV-12%) while chronic GVHD in 14% patients (grade III/IV-4%). Eighty eight patients (71%) are alive and disease free at a median follow-up of 223 days (range, 55â€“1213 days). Transplant related mortality was 28/124 (22%). Causes of these deaths were infection-18, GVHD-7, regimen related toxicity-3. Eight patients died due to relapse and/or progressive disease. CONCLUSIONS: Our results are comparable to the reports from developed countries in terms of complications and outcomes of the treatment. This gives hope to many children who need allogeneic stem cell transplant in the developing world. Keywords: allogeneic, children, stem cell transplant, outcome Conflicts of interest: none

213. Prevalence and hematological profile of Î²-thalassemia and sickle cell anemia in four communities of Surat city

2012

Indian Journal of Human Genetics

Bhukhanvala, D and Gupte, S and Patel, A and Shah, A and Sorathiya, S

Background: From the data of transfusion-dependent thalassemia major cases, the 4 communities (Muslim, Dhodia Patel, Kachhiya Patel, and Modh Bania) with high prevalence but not studied methodically were selected. Aim: The aim of this study is to find prevalence of -thalassemia and sickle cell anemia in 4 selected communities and also to evaluate hematological profile in them. Materials and Methods: For screening of -thalassemia trait (BTT) and sickle cell trait (SCT), all samples were tested for red cell indices, solubility, HbA 2 level and doubtful cases confirmed on HPLC. Statistical Analysis: Mean SD, 2 and â€²tâ€² tests were used to evaluate the significance. Results and Conclusion: Among 4 selected communities, the highest prevalence of BTT was observed in Modh Bania (6.2%) and Kachhiya Patel (6.05%) and that of SCT in Dhodia Patel (14.0%). Significantly higher prevalence of BTT was observed in Memon (P < 0.0001) and of SCT in Khalifa 6.6% (P < 0.0001) compared to other Muslim sub castes. Anemia was more prevalent in BTT compared to non-BTT and non-SCT subjects. 80% of Dhodia Patel non-BTT and non-SCT subjects showed microcytic red cell morphology. Their Mean SD Hb concentration was 12.1 1.73, hence iron deficiency cannot be a sole reason. This community needs -thalassemia and iron studies.

214. Allogeneic stem cell transplantation in children: Single centre experience from north India

2019

Bone Marrow Transplantation

Vyas, C and Singh, N and Ansari, F and Dayama, A and Kurmi, S and Bhargava, R and Dua, V

Background: Allogeneic stem cell transplant (Allo-SCT) services in children are still far behind in India as compared to the developed countries because of the resource constraints. There is a paucity of literature for the same from developing world. We present our experience of Allo-SCT for various benign and malignant paediatric diseases. Methods: A retrospective analysis of total 101 children (61 male and 40 female) who underwent allo-SCT between January 2014 and May 2017 at a tertiary care hospital in North India was done. The mean age of the patients was 9.2 years (range: 14 months-17 years). The indications for benign diseases were hemoglobinopathy [thalassemia major (TM)-22, sickle cell disease(SCD)-6], aplastic anemia-16, Fanconi anaemia-10, Diamond-Blackfan anemia-1, immunodeficiency (mucopolysaacharidoisis-2, one each for Wiskott-Aldrich syndrome and Chediak-Higashi syndrome), while for malignancies were acute myeloid leukaemia (AML)-14, acute lymphoblastic leukaemia (ALL)-20, juvenile myelomocytic leukaemia (JMML)-1, myelodysplastic syndrome-1, relapse neuroblastoma-1 and chronic myeloid leukaemia (CML)-5. Donors were HLAmatched sibling-58, haploidentical-33, single antigen mismatch-5 and matched unrelated-5. The source of stem cells was peripheral blood in 98 patients and bone marrow in 3 patients. We chose a post-transplant cyclophosphamide based approach in majority of haploidentical transplants except in 4 patients, where T cell receptor alpha beta CD 19 depletion was done. Results: Out of total 101 patients, 70 patients are alive and disease free at a median follow-up of 223 days (range: 55-1213 days). The median time for neutrophil engraftment was at day 13 (range: 11-18 days) in 96/101 patients, including 5 patients who underwent second allo-SCT. Five patients had rejection (one each with TM, SCD, AML, CML and JMML), out of which 2 patients are alive and disease free. Acute graft versus host disease (GVHD) was reported in 31% patients (grade III/IV-12%) while chronic GVHD in 14% patients. Day 100 mortality was 31/101 (30%). Causes of non relapse mortality were infection-18, GVHD-5, veno-occlusive disease-1. Seven patients died due to relapse and/or progressive disease. None of the patients succumbed to cytomegalovirus, BK virus, Epstein-Barr virus or adenovirus disease. Conclusions: Our results are comparable to many national and international published reports in terms of

complications and outcomes of the treatment. This gives hope to many children who need allogeneic stem cell transplant in the developing world.

215. Methylenetetrahydrofolate reductase polymorphisms as genetic markers to predict homocysteinemia and clinical severity in sickle cell disease

2021

Biomarkers in Medicine

Patel, S and Nanda, R and Hussain, N and Mohapatra, E and Patra, P K

Aim: The present study observed the relationship between the methylenetetrahydrofolate reductase genotypes and clinical outcome in children with sickle cell disorder. Methodology: A total of 249 children were recruited for the study and evaluated clinically for calculating severity score, homocysteine levels and C677T and A1298C genotyping. Results: The frequencies of variant genotypes were 28.1% CT/TT677 and 69.1% AC/CC1298. Plasma homocysteine was significantly elevated in variant groups ($p < 0.001$). Both the genotypes accorded significant association with homocysteinemia ($p < 0.001$). Vascular crisis ($p = 0.04$), frequency of hospitalization ($p < 0.001$) and severity score ($p = 0.02$) revealed association with C677T and not with A1298C. The CT/TT677 genotypes showed 3.39-times ($p = 0.032$) increase in a higher score for severity. Conclusion: C677T depicted significant association with clinical severity in study population.

216. Assessment of Impact of Hematopoietic Stem Cell Transplant on Sickle Cell Disease Burden Index

2017

Bone Marrow Transplantation

Kharya, G and Agarwal, S and Waiswa, M and Sola, O and Kasirye, E

Introduction: Sickle cell disease (SCD) poses a lot of psychological burden for the patient and the caregiver. It also poses a significant financial burden over the family. Ohaeri et al developed a 16 point questionnaire to asses sickle cell disease burden called as sickle cell disease burden index (SCDBI) and its impact on caregiver's quality of life (QOL). We used this questionnaire to assess the impact of hematopoietic stem cell transplant (HSCT) on caregiver's QOL. Material and Methods: 16 point questionnaire was sent to 15 set of parents whose child underwent HSCT between Jan 2016 and June 2016. SCDBI contained 16 questions in various domains (3:family finances, 3:family interactions, 5:routine family activity and 5:parental coping ability). Answers were graded on a score of 0-3 (0:never occurred and 3:occurred regularly or had a severe impact on the family). The results were interpreted in two headings A. family finances and interactions (0:no impact 1-3:insignificant impact 4-6:moderate impact 7-9:severe impact) and B. routine family activity and parental coping ability (0:no impact 1-5:insignificant impact 6-10:moderate impact 11-15:severe impact). All these domains were assessed before and after HSCT. Result: Ten parents replied with duly filled questionnaire. Mean age at HSCT was 8.1 years (range 1-14), M/F:7/3. All were symptomatic for >6 months before HSCT with 90% having more than 2 hospital admissions. Majority of parents were from middle class with median family income of 30000 USD per annum (range 16000-200000 USD). Median score for family finances and interactions (A) before HSCT was 6 (range 1-19) which decreased to 0 (range 0-3) after HSCT. Median score for routine family activities and parental coping ability (B) before HSCT was 13 (range 3-25) which decreased to 0 (range 0-6) after HSCT. Conclusion: Our results suggest that before HSCT there was a moderate impact on family finances and interactions which reduced to no impact after HSCT. Similarly there was severe impact on family activities and parental coping ability before HSCT which changed to no impact after HSCT. Our study suggests that HSCT not only improves the QOL of the child but also of the caregivers.

217. HB electrophoresis as a diagnostic tool for detection of sickle cell disease in tertiary care centre

2020

Indian Journal of Hematology and Blood Transfusion

Saxena, S and Singh, U and Saxena, P

Aims & Objectives: To determine the prevalence of undiagnosed cases of sickle cell disease in the society. Patients/Materials & Methods: OPD & IPD patients from departments of internal medicine, surgery, Ortho and Pediatrics with moderate to severe anemia suspected for sickle cell disease, at Index Medical College and Hospital, Indore, from the month of June 2019 to March 2020 were included in study. Sickling test was conducted on them and Hemoglobin electrophoresis was performed to confirm for presence of Sickle cell disease. Results: Out of 109 samples included in study, 58 (53.2%) cases were positive on sickling test & 51 (46.7%) showed sickle test negative. On Hb electrophoresis, 69(63.3%) cases were positive for sickle cell disease. Discussion & Conclusion: Sickle Cell disorders has wide spread presence in different tribes of Central India. Individuals with sickle cell trait have shown to develop sickling which leads to organ damage when they are exposed to hypoxia, excessive exercise, high altitude, dehydration etc. Genetic counselling should be offered to all adoloscents at risk of transferring the sickle cell disease to offsprings.

218. Allogeneic stem cell transplantation in children: Single centre experience from north India

2018

Pediatric Blood and Cancer

Vyas, C and Ansari, F and Pandit, A and Singh, N and Dua, V

Background/Objectives: Allogeneic stem cell transplant (Allo-SCT) services in children are still far behind in India as compared to the developed countries because of the resource constraints. We present our experience of Allo-SCT for various benign and malignant paediatric diseases. Design/Methods: A retrospective analysis of total 101 children (61 male and 40 female) who underwent allo-SCT between January 2014 and May 2017 at our centre was done. The mean age of the patients was 9.2 years (range, 14 months-17 years). The indications for allo-SCT were hemoglobinopathy [thalassemia major(TM)-22, sickle cell disease(SCD)-6], aplastic anemia-16, Fanconi anaemia-10, Diamond-Blackfan anemia-1, immunodeficiency (mucopolysaacharidoisis-2, one each for Wiskott-Aldrich syndrome and Chediak-Higashi syndrome), acute myeloid leukaemia (AML)-14, acute lymphoblastic leukaemia (ALL)-20, juvenile myelomocytic leukaemia (JMML)-1, myelodysplastic syndrome-1, relapse neuroblastoma-1 and chronic myeloid leukaemia (CML)-5. Donors were HLA-matched sibling-58, haploidentical-33, single antigen mismatch-5 and matched unrelated-5. The source of stem cells was peripheral blood in 98 patients and bone marrow in 3 patients. We chose a post-transplant cyclophosphamide based approach in majority of haploidentical transplants. Results: Out of total 101 patients, 70 patients are alive and disease free at a median follow-up of 223 days (range, 55-1213 days). The median time for neutrophil engraftment was at day 13 (range, 11-18 days). Five patients had rejection (one each with TM, SCD, AML, CML and JMML). Acute graft versus host disease (GVHD) was reported in 31% patients (grade III/IV-12%) while chronic GVHD in 14% patients (grade III/IV-4%). Day 100 mortality was 31/101 (30%). Causes of non relapse mortality were infection-18, GVHD-5, veno-occlusive disease-1. Seven patients died due to relapse and/or progressive disease. Conclusions: Our results are comparable to the reports from developed countries in terms of complications and outcomes of the treatment. This gives hope to many children who need allogeneic stem cell transplant in the developing world.

219.Public health challenges of sickle cell disorders, beta-thalassemia syndrome and G6PD deficiency.

2014

India: Health and human development aspects.

Balgir, Ranbir S

This reprinted article originally appeared in Public health yearbook, Healthand human development, 2011, 337-350. The following abstract of the original article appeared in (see record 2013-16532-026).The undivided state of Madhya Pradesh is inhabited by 46 tribal communities in Central India that constitute about 23% tribal population of India. This randomly conducted study presents the public health challenges of sickle cell disorders, beta-thalassemia syndrome and G6PD deficiency in relation to malaria endemicity in scheduled caste and tribal communities of Chhattisgarh and Madhya Pradesh in Central India. High prevalence of the sickle cell disorders was recorded in tribes of Baiga (22.3%) and Bharia (13.2%) with a range of beta-thalassemia trait being 0-3.6% in Madhya Pradesh, followed by Hill Maria (22.5%), Maria (20.2%) and Muria (14.9%) tribes with beta-thalassemia trait range of 0-10.4% in Chhattisgarh. The G6PD deficiency was varying from 0% to 21.5% in Chhattisgarh and from 1.8% to 12.1% in Madhya Pradesh. The frequency of sickle cell disorders fluctuated between 4.1% to 34.0% among the scheduled tribes of Madhya Pradesh and between 0.9% to 22.5% in scheduled tribes of Chhattisgarh. The range of beta-thalassemia trait was variable from 0% to 10.4% in Chhattisgarh and from 0% to 10.0 percent among the scheduled tribes of Madhya Pradesh. The G6PD deficiency range was 1.3% to 9.3% among the scheduled tribes and 0% to 6.9% in scheduled castes of Madhya Pradesh. Among the scheduled castes, the frequency of sickle cell disorders varied from 4.4% to 37.9%, the sickle cell-beta-thalassemia being 3.9%. The frequency of beta-thalassemia trait was variable between 0 to 10.0 percent among the scheduled castes of Madhya Pradesh. (PsycINFO Database Record (c) 2016 APA, all rights reserved).

220.Priapism in sickle cell disease.

2016

Sexuality: Some international aspects.

Balgir, Ranbir S

The sickle cell hemoglobinopathy is a common disabling disease profoundly affects human morbidity, mortality and quality of life. Priapism in sickle cell disease is a condition that cause sustained, painful, and unwanted erection of the penis in boys or men without any sexual stimulation. Sickled cells are short lived and can cause vaso-occlusive crisis in affected persons. A few case reports from India have shown the rare occurrence of priapism in sickle cell disease in India. The present cross-sectional and hospital based study showed around 3% (2.97%) prevalence of priapism in cases suffering from sickle cell disease in a tertiary hospital at Jabalpur in Madhya Pradesh of Central India. It is a common practice in India that any problem related to sex or sex organs is intentionally not disclosed (kept secret) to elderly family members because of shyness or psycho-social implications or due to a stigma attached to it. It is never brought to the notice of a medical doctor. This is due to utter lack of sex education in rural areas, resulting in deteriorated sexual health and related complications. Priapism in sickle cell disease is a pathological condition of penile erection and recovery of the erectile function is dependent on prompt counseling and urgent intervention. Priapism in sickle cell disease should be considered as a medical and surgical emergency and should not be taken as lightly or ignored. (PsycINFO Database Record (c) 2019 APA, all rights reserved)

221.Hemoglobinopathy in India

2015

Clinica Chimica Acta

Iyer, S and Sakhare, S and Sengupta, C and Velumani, A

Objectives: Variations in hemoglobin structure as well as number of globin chains give rise to a wide spectrum of heritable disorders. As such, their detection is significant from epidemiological perspective, especially in India in which there is a large multi-cultural population with distinct geographic distribution. Although a few variants present severe clinical symptoms in homozygotes, co-existence of heterozygous mutants can lead to deleterious conditions. The aim of the present study is to provide an overview on the prevalence of different hemoglobinopathies among Asian Indians. Design and methods: A large cohort of samples from all regions of India was analyzed by high performance liquid chromatography (HPLC) (n= 25,297) and capillary electrophoresis (CE) (n= 21,219). Results: Using HPLC, 8029 hemoglobin variants were detected. HbS trait was detected at the highest frequency (33.03%), principally from the Chattisgarh region. Using CE, 6524 variants were detected. HbS trait, again, represented the most common mutation (25.67%). A total of 40 variants including compound heterozygous cases were detected by HPLC and CE. Conclusions: Our report is one of the few to analyze a large cohort and report on the spectrum of hemoglobin variants in India.

222. A cross sectional study on sickle cell disease among backward communities of Gadchiroli, Maharashtra, India

2014

Indian Journal of Public Health Research and Development

Samal, J and Meshram, F A

Aim of the study: To assess the prevalence of sickle cell disease among various backward communities of Gadchiroli district. Methodology: The study is based on Solubility test, a laboratory investigation method used for the diagnosis of sickle cell disease. The tests were conducted in a stall opened at Agrotech-2011 on Dec 27-29, a state level agrotech festival. Observation and Discussion: The total sample used for the study was 560, out of which 75.89% are male and 24.10% are female. Category wise populations in the study are OBC-40.53%, SC-25.35%, ST-20%, Open-2.67%, SBC-2.14%, and NT-8.75%. Among 560 samples tested using solubility test 69 (12.32%) samples are found positive out of which 28.98% are female and 71.01% are male. The caste wise distribution of solubility test confirmed samples are SC-36.23%, ST-26.08%, OBC-24.63%, NT- 13.04%, SBC-0, Open-0. Conclusion and Recommendation: The study concludes that the prevalence of sickle cell disease among backward classes in Gadchiroli district is more in comparision to general or open category. The district is rich in tribal and other related backward communities, so prevention, control and management of sickle cell disease should be a priority of the health department. Endogamy and consanguineous marriage is one of the important factors for the perpetuation of the disease among tribal communities. Proper IEC activities need to be implemented to address this issue.

223. Spectrum of hemoglobinopathies in Eastern Uttar Pradesh

2009

Indian Journal of Pediatrics

Gupta, V and Shukla, J and Tilak, V and Bhatia, B

224. Prevalence of Helicobacter pylori-associated peptic lesions among patients with sickle cell disease with recurrent abdominal pain

2008

Indian Journal of Gastroenterology

Karimi, M and Haghighat, M and Moemen, T and Jamalian, N

225.Status of HbE variant among rabha tribe of west Bengal, India

2015

Indian Journal of Medical Research, Supplement

Bhattacharyya, D M and Basak, J and Mukhopadhyay, S and Mukhopadhyay, A

226.Hepatic manifestations in sickle cell disease.

1992

Indian pediatrics

Mishra, S and Thapa, B R and Yachha, S K and Malik, A K and Mehta, S

227.Osseous manifestations in sickle cell anemia.

1969

Indian journal of pediatrics

Shivde, A V and Rao, V

228.Prevalence of hemoglobinopathy, ABO and rhesus blood groups in rural areas of West Bengal, India

2012

Journal of Research in Medical Sciences

Mondal, Bikash and Maiti, Soumyajit and Biswas, Biplab Kumar and Ghosh, Debidas and Paul, Shyamapada

229.Do gender differences influence the prevalence of sickle cell disorder and related morbidities among school children in rural central India?

2013

International Journal of Collaborative Research on Internal Medicine & Public Health

Charuhas, Akre V and Neelam, Sukhsohale D and Sanjay, Kubde S and Sanjay, Agrawal B and Mohan, Khamgaokar B and Sanjeev, Chaudhary M and Manjusha, Dhoble A

230.Sickle cell anaemia in India.

1952

Indian medical gazette

231. Variable phenotypes of sickle cell disease in India with the Arab-Indian haplotype

2015

British Journal of Haematology

Italia, K and Kangne, H and Shanmukaiah, C and Nadkarni, A H and Ghosh, K and Colah, R B

232. Genetics and epidemiology of sickle cell anemia in India.

1988

Indian journal of medical sciences

Rao, V R

233. Sickle cell gene in the Mina tribal population of Kherwara tehsil of Udaipur district in Rajasthan.

1983

The Indian journal of medical research

Jain, R C and Andrew, A M and Choubisa, S L and Acharya, A and Joshi, K C

234. ABO blood groups and sickle-cell trait investigations in Madhya Pradesh, Indore District (Central India).

1966

Acta geneticae medicae et gemellologiae

Kumar, N

235. Sub-division of some Southern Indian communities according to the incidence of sickle-cell trait and blood groups.

1952

Transactions of the Royal Society of Tropical Medicine and Hygiene

LEHMANN, H and CUTBUSH, M

236. Hb.S-thalassaemia disease in India.

1958

Journal of the Indian Medical Association

Chatterjea, J B and Swarup, S and Ghosh, S K and Ray, R N

237.Red cell genetic abnormalities in the tribes of five districts of Madhya Pradesh.

1987

The Indian journal of medical research

Sathe, M and Gorakshakar, A C and Rao, V R and Mukherjee, M and Vasantha, K and Bhatia, H M

238.Homozygosity for a haplotype in the HBG2-OR51B4 region is exclusive to Arab-Indian haplotype sickle cell anemia

2016

American Journal of Hematology

Vathipadiekal, V and Alsultan, A and Baltrusaitis, K and Farrell, J J and Al-Rubaish, A M and Al-Muhanna, F and Naserullah, Z and Suliman, A and Patra, P K and Milton, J N and Farrer, L A and Chui, D H K and Al-Ali, A K and Sebastiani, P and Steinberg, M H

239.Incidence of sickle cell disease in Chandrapur area.

1983

Indian journal of medical sciences

Bobhate, S K and Kabinwar, N and Sonule, SS

240.Haemoglobin-S in Agharia community of Orissa.

1967

Journal of the Indian Medical Association

Nanda, B K and Panda, G K and Naik, U P and Nankda, C N and Prharaj, K C

241.Sickle cell disease in India.

1958

Blood

Shukla, R N and Solanki, B R and Parande, A S

242.Deficiency of erythrocyte glucose-6-phosphate dehydrogenase and sickle cell trait: a survey of Mahar students at Aurangabad, Maharashtra.

1968

The Indian journal of medical research

Deshmukh, V V and Sharma, K D

243.Sickle-cell trait in Central India.

1958

Lancet

Shukla, R N and Solanki, B R

244.Sickle cell disease: Status with particular reference to India

2016

Indian Journal of Medical Research

Rees, D C and Brousse, V A M

245.Milder clinical course of sickle cell disease in patients with Î± thalassemia in the Indian subcontinent

1997

Blood

Mukherjee, M B and Colah, R B and Ghosh, K and Mohanty, D and Krishnamoorthy, R

246.Clinical diversity of Sickle cell disease in Western India - Influence of genetic factors

2000

Acta Haematologica

Mukherjee, M B and Surve, R R and Ghosh, K and Colah, R B and Mohanty, D

247.Sickle cell anaemia in Assam.

1958

Journal of the Indian Medical Association

Batabyal, J N and Wilson, J M

248.Sickle-cell anaemia in an Indian family in Malaya.

1959

The Medical journal of Malaya

VELLA, F and HART, P L

249. Sickle-cell trait in southern India.

1952

British medical journal

Lehmann, H and Cutbush, M

250. The occurrence of sickle cell anaemia among a group of tea garden labourers in Upper Assam.

1952

Indian medical gazette

Dunlop, K J and Mozumder, U K

251. Prevalence of sickle cell disease among children of tribal population in India: Feasibility of screening at community level in lowâ€resource settings.

2021

Pediatric Blood & Cancer

Babu, Bontha V and Sridevi, Parikipandla and Surti, Shaily and Ranjit, Mano R and Bhat, Deepa and Sarmah, Jatin and Sudhakar, Godi and Sharma, Yogita

252. Prevalence of haemolysis in peripheral blood smear in cases of megaloblastic anemia

2006

Medical Journal Armed Forces India

Kinra, P

253. Tackling the Menace of Anemia and Hemoglobinopathies among Young Adults -- Conceptualizing University-Level Screening.

2021

Indian Journal of Community Medicine

Patel, Geetika Madan and Parmar, Ankita and Zalavadiya, Dhara and Talati, Kandarp

Background: National family health survey-4 data suggests alarmingly high prevalence of anemia among adult population. Hemoglobinopathies such as thalassemias and structural hemoglobin (Hb) variants are the commonly seen autosomal, recessively inherited, monogenic disorders of Hb production, and pose a significant health burden in India. Premarriage screening for thalassemia would help to prevent such marriage, reduce health and financial burdens. Objectives: To assess the burden of anemia and hemoglobinopathies, among newly admitted college students through a University-level screening program. Methodology: A cross-sectional study was conducted among college students of the University. The study was part of regular health check-up of all new admissions.

Sample frame included all the 4197 students who appeared for health screening and were screened for anemia and hemoglobinopathies. Results: Out of 4197 students, 73.2% were male and a total of 19.5%were anemic. Gender-wise prevalence among males and females was 13.6% and 35.7%, respectively. Among anemic, the proportion of mild, moderate, and severe anemia was 69%, 29%, and 2%. Prevalence of typical beta thal minor and sickle cell trait was found to be 2.6% and 1.4%. Conclusions: Anemia and hemoglobinopathies are significant public health challenges. University setup offers a unique opportunity for modeling and pilot testing integrated interventions for screening and management.

254.To study the haemoglobinopathies and ratio of copper and zinc in Sindhi Community of Bhopal

2013

International Journal of Pharma and Bio Sciences

Kaur, M and Dangi, C B S and Singh, H

The genetic haemtological disorder such as beta-thalassaemia and sickle cell anaemia is one of the burning problems in India. The community wise study is of great help as it provides versatile information. A random cross-sectional study was conducted in 500 volunteers of Sindhi community belonging to all age groups and both sexes. The mass screening was done by help of NESTROFT, Sickling, Solubility and complete blood picture were performed on all samples along with BMI .Those positive for either one or both, screening tests were further analyzed for HbA2 by HPLC D-10. 120 positive cases of haemoglobinopathies were further analyzed for copper /zinc ratio. 120 positive cases of haemoglobinopathies were having low level of zinc and high level of copper, the ratio of copper/zinc was high along with low BMI. The positive cases were having different clinical manifestations along with liver and heart diseases in some cases.

255.Sickle cell disease in Northwestern India. A retrospective study

2011

Indian Journal of Hematology and Blood Transfusion

Rajaguru, P and Jain, R and Das, R and Trehan, A and Bansal, D and Malhotra, P and Marwaha, R K and Varma, S and Garewal, G

Introduction: Sickle cell disease (SCD) is an uncommon disease in the northwestern belt of India. Most of the cases presenting to our institute are referral cases. The patients have varying age and different symptoms at presentation. Based on parental screening they are classified into homozygous SCD, heterozygous sickle cell trait (SCT), double heterozygous sickle cell Î² thalassemia (SÎ²) and double heterozygous sickle cell HbD disease (SD). In this study, retrospective analysis of the hematological parameters in sickle cell disease patients was carried out. Materials & Methods: Data were collected from the archives for a period of 14 years (1996-2000). Clinical data as well as laboratory data such as hemoglobin, MCV, MCH, RDW, RBC count, peripheral blood picture, HbF values, hemoglobin electrophoresis and HPLC data were collected. Results: Total number of cases encountered was 150. Homozygous SCD (n = 20)-13%, heterozygous SCT (n = 77)-51.3%, SÎ² (n = 27)-18%, HbSD disease (n = 9)-6% and in 12 patients definite diagnosis was not made as parental screening was not available. 54.6% cases were males and 45.4% were females, however 65% were males and 35% females among patients of homozygous SCD and 70.4% males and 29.6% females among patients of double heterozygous SÎ²T. Peripheral blood picture was available for 144 patients of which only 28 patients had sickle cells (19%). Mean age of presentation of Homozygous SCD was 6 years (1.5-10), mean Hb was 8.7 g/dl (5.7-12.1). Mean red cell indices were MCV 85.3 fl, MCH 27.3 pg, RDW% 18.19 and HbF% 17.5, HbS% 73.9. Age of presentation of SÎ²T was 12 years (1.5-20 years), Hemoglobin 7.8 g/dl (4.3-10.8), MCV 74.5 fl, MCH 23.3 pg, RDW 23%, HbF% 20.5 (10.8-48), HbS% 69.8, HbA 6.4%, HbA 2% 5.1. Conclusion: SCD is an uncommon problem in this region and parental screening is essential for definite classification of the various subgroups of SCD.

256. Study of blood groups and haemoglobin variants among the Santal tribe in Midnapore District of West Bengal, India.

1967

American journal of physical anthropology

Chaudhuri, S and Ghosh, J and Mukherjee, B and Roychoudhury, A K

SCREENING AND DIAGNOSIS

1. **Universal implementation of newborn screening in India**

   2020

   International Journal of Neonatal Screening

   Mookken, T

Newborn screening is a successful program in many developed countries. In India, the benefits of dried blood spot screening have been recognized and that screening is slowly gaining traction. There are significant issues standing in the way of universal implementation of a newborn screening program in India: awareness, cost, advocacy, public policy, and politics. Three regional screening programs, Chandigarh, Goa, and Kerala could serve as models for other programs in India. The data for this commentary were based on personal experiences from managing public newborn screening programs, searches on PubMed and Google, and personal interactions with experts in the field. The overwhelming recommendation is to universally screen for congenital hypothyroidism in India, because it is easy and inexpensive to treat, with excellent outcomes. It would also be beneficial to consider screening universally for glucose-6-phosphate dehydrogenase deficiency due to its high incidence and ease of treatment. Finally, sickle cell disease should be screened in those areas in India where it is prevalent due to the costs associated with universal screening. Achieving universal screening is a challenge, and it is very difficult to predict when every baby born in India will be screened for at least congenital hypothyroidism.

2. **Capnia Awarded NIH Grant to Develop Sickle Cell Anemia Screening in Developing Countries**

   2015

   Clinical Lab Products (Online)

The 6-month SBIR grant will be used to help fund the development of a modified CoSense device that is suitable for field use in developing countries with high prevalence of sickle cell disease (SCD), also known as sickle cell anemia (SCA).

3. **Newborn screening for sickle cell disease & congenital hypothyroidism in western Orissa**

   2011

   Indian Journal of Hematology and Blood Transfusion

   Mohanty, D and Das, K and Misra, K and Investigator, P

Introduction: New Born Screening (NBS) is in application as national health programme in many developed countries. Sickle cell disease (SCD) and congenital Hypothyroidism (CH) has been indexed under the newborn screening programme in USA and UK and the outcome of these programmes are remarkably successful in minimizing the disease course by a long-term strategy for management and health care provisions. In India screening for sickle cell disorders are limited mostly to retrospective and subjective detection of cases. Population based screening with an aim to provide health care and treatment-management are yet to be established although states with earmarked populations at risk (Madhya Pradesh, Chhattisgarh, Maharashtra and Orissa) have been documented where the frequency ranges from 5 to 35%. The present programme was undertaken in western Orissa to implement NBS and continue a reach-out strategy for detection, follow up, treatment-management for SCD and CH and to develop relevant awareness among people. Method: Newborns aging 7-45 days are enrolled from two blocks of Kalahandi district of western Orissa after getting written consent from their parents. 5 l heel-prick

blood is analysed to detect presence of sickle cell haemoglobinopathies and other abnormal haemoglobins if any by HPLC method using Variant II platform (Bio-Rad Laboratories, Hercules, USA). Dry blood spots collected by standard method using Multipart Guthrie card (S & S 903 filter cards, Whatman Inc., USA) are transported back to the laboratory for detection of TSH level using ELISA based neonatal TSH kit (Bio-Rad Laboratories UK, Perth). TSH level higher than 15 UI/ml was considered elevated and the baby is retested thrice with 15 days interval to record TSH level. Serum T3 and T4 are tested for confirmation of hypothyroidism in babies with consistent elevated neonatal TSH level. All babies tested were given genetic cards with the status of sickle cell disorder and CH. Newborn detected to have SCD are registered and are under regular monitoring. Prophylaxis penicillin is started for all SCD babies from 6 months of age. Results: Between August 2009 and July 2010, 1,668 newborns have been enrolled and screened for SCD and CH. An average incidence of 17.62% of Sickle cell trait (HbAS) is recorded for the area with the highest incidence observed in the tribal dominated part (19.03%). The data till date reveals a striking fact that more than 20 per thousand live births in the district are born with the disease. All the 34 cases of SCD detected were confirmed by parents testing, of which confirmation of 4 cases of compound heterozygosity for HbS and thalassaemia is an interesting finding. The sole case of CH (with TSH value>80 UI/ml) is responding progressively under LT4 treatment with a dose of 6 g/kg wt and close monitoring. Clinical and quantitative observations are being made periodically. A general trend of increasing awareness regarding the sickle cell disease is observed among the local people with willing participation. It is heartening to note that the interaction and community participation is increasing. Conclusions: The design of the programme provides scope for catering the benefit of the NBS in rural western Orissa and follow up for newborns with SCD and CH in the area where, more than half of population is living below poverty line and the rate of literacy is poor. In the current context of the health provision in this area and the available infrastructure pertaining to the detection of SCD and CH, availing this benefit was otherwise not workable and long term planning with structured intervention are seemingly not in existence. Our effort in this programme rests on a defined three layered strategy involving base-line health workers, district health network and community level participation coalesced with advanced laboratory detection facilities and systematic follow up. The programme advocates the acute need of such kind of extensive reach-out programme for early and confirmed detection of SCD and CH to be undertaken by the Government of the state in long term basis to reduce the child mortality and morbidity due to these disorders.

4. **Evaluation of a capillary blood collection system for screening for hemoglobinopathies in remote areas**

   2010

   International Journal of Laboratory Hematology

   Colah, R B and Wadia, M and D'Souza, E and Sawant, P M and Mohanty, D and Mehra, M

Accurate estimation of hemoglobin (Hbs) A, Hb A2,HbFandabnormal Hb is required for diagnosis of hemoglobinopathies and genetic counseling. High pressure liquid chromatography (HPLC) is the most suitable approach available. But for 70% of the rural Indian population, HPLC analysis facilities are not available and screening would require transportation of samples to laboratories in bigger cities. We thus evaluated the feasibility of using a kit designed for measuring Hb A1c using capillary blood for collection and preservation of samples over a period of 15 days at different temperatures for screening for hemoglobinopathies. Capillary blood (5 Î¼l) of 90 individuals was collected in the capillary collection system and run on the Variant HemoglobinTestingSystemondays1,3,5,8,12and15 after incubation at 4, 22, 37, 42 and 50 Â°C. The stability of different Hbs varied at different temperatures. The stability was maintained for 12 to 15 days by most of the samples up to 37 Â°C. Hb E was stable for 3 days up to at 37 Â°Cand Hb Dand Hb Qfor 3 daysupto42 Â°C. This capillary blood collection system would have tremendous potential for sample collection and transportation under adverse climatic conditions for screening of hemoglobinopathies in remote areas in different countries. Â© 2008 Blackwell Publishing Ltd.

5. **Population screening and prevention strategies for thalassemias and other hemoglobinopathies of Eastern India: Experience of 18,166 cases**

   2015

   Hemoglobin

   Chatterjee, T and Chakravarty, A and Chakravarty, S

We evaluated population screening programs (1999-2011), conducted by the Thalassaemia Foundation, Kolkata, India, for the first time in Eastern India in different districts of West Bengal, for prevention of thalassemia comprising screening of heterozygotes and Î²-thalassemia intermedia (Î²-TI) cases [Î²+, Î²++, Î²0/Î²+, Î²E/Î²E (codon 26 or HBB: c.79G > A), Hb-E-Î²-thalassemia (Hb E-Î²-thal)]. Among 18,166 cases, we found 2092 heterozygotes and 2245 Î²-TI individuals (who had no information about their disorders). Results were evaluated with standard hematological analyses including erythrocyte indices, hemoglobin (Hb) typing and quantification. Participants were divided into five groups (children, pre-marriage cases, pre-pregnancy cases, affected family members, pregnant women). The objectives of this evaluation were to fix cut-off values of red blood cells (RBCs), mean corpuscular volume (MCV), mean corpuscular Hb (MCH), red blood cell distribution width (RDW) and Hb A2, as the standard World Health Organization (WHO) guidelines were not strictly followed in mass-scale screening programs. We have observed many dilemmas in considering the status of the thalassemia subject, due to presence of some other clinical conditions such as iron deficiency anemia, Î±-thalassemia (Î±-thal), Î´-thalassemia (Î´-thal), clinically silent Hb variants, and some cases of non hemoglobinopathies (such as pregnancy) along with thalassemia. The MCV values varied greatly in different conditions of hemoglobinopathies, whereas MCH provided a more stable measurement. We found an MCH value of <27.0 pg is a suitable cut-off point for screening in this population. Participants with an MCH of <27.0 pg should be investigated further to confirm or exclude a diagnosis of Î²-thal trait.

6. **Newborn Screening: Need of the Hour in India**

   2015

   Indian Journal of Pediatrics

   Verma, I C and Bijarnia-Mahay, S and Jhingan, G and Verma, J

After a review of the current health scene in India, the authors suggest that the Government of India should consider seriously, the introduction of new born screening. As a first step, a central advisory committee should be constituted to recommend what is required to be done to strengthen the infrastructure and the manpower to carry out new born screening, and the disorders to be screened. In the urban hospitals newborn screening (NBS) for three disorders can be easily introduced (congenital hypothyroidism, congenital adrenal hyperplasia and G-6-PD deficiency), while in the rural areas this should begin with congenital hypothyroidism, especially in the sub Himalayan areas. Concurrently, logistic issues regarding diets and special therapies for inborn errors of metabolism should be sorted out, laboratories to confirm the diagnosis should be set up, and a cadre of metabolic physicians should be build up to treat those identified to have inborn errors of metabolism. Once these are established on a firm footing, tandem mass spectrometry should be introduced as it allows the identification of a number of disorders in an affordable manner. The recent improvements and current trends in health care in India have created the necessary infrastructure for adopting NBS for the benefit of infants in India.

7. **Significance of Low HbA2 levels and correlation with serum iron profile**

   2016

   Indian Journal of Hematology and Blood Transfusion

   Gudapati, P and Manohar, C

Introduction and Background: Haemoglobin HbA (Î±2Î²2) is the main haemoglobin component in postnatal life, accounting for>96 % of total Hb, followed by HbA2 (Î±2Î´2) representing 2.5-3.5 %, and HbF (Î±2Î³2)

constituting <1 %. Decreased HbA2 levels can be detected in iron depletion, due to the preferential binding of Î² to Î± chains, rather than Î´ chains, or to an inhibition of low iron levels on d globin synthesis. Other causes of low HbA2 include Î±Î² thalassemia, HbH disease, Hb lepore, Î± chain variants etc. Material and Methods: Haemoglobin Electrophoresis reports were reviewed for a period of 2 years 6 months (Jan 2014 to June 2016) from archives at Hematology & Clinical Pathology laboratory, Kasturba hospital, Manipal University, Manipal. Data from patient records with low HbA2 (defined as <2.2) was collected which included serum iron profile, RBC indices and peripheral smear findings and correlated. Haemoglobin electrophoresis is performed using Sebia capillary electrophoresis. Patients without serum iron profile were excluded from the study. Results: Total 127 patients were having HbA2 levels <2.2, out of which 26 cases were excluded in view of no serum iron profile. Out of remaining 101 cases, 58/101 had serum iron profile suggesting Iron deficiency anaemia with low iron, high TIBC and low ferritin. 4/101 patients had high HbS and high Hbf along with low Hba2 and diagnosed as sickle thalassemia. 2 cases of sickle cell trait and one case of sickle cell anaemia as well showed low Hba2. Also included in study were 2 cases of thalassemia intermedia, 3 cases of thalassemia major, 2 cases of Î± thalassemia minor and one case each of HbH disease and db thalassemia. 26/101 cases had normal iron profile and their RBC parameters were studied. Conclusions: Majority of cases with low HbA2 were having iron deficiency anaemia and other causes included various hemoglobinopathies with defective Î± and Î´ chain binding.

8. **Research journal of pharmaceutical, biological and chemical sciences: Naked eye single tube red cell osmotic fragility test screening for detection of B-Thalassemia trait-an evaluation against HPLC Method at Rajendra Institute Of Medical Sciences, Ranchi**

   2014

   Research Journal of Pharmaceutical, Biological and Chemical Sciences

   Prasad, C and Singh, S B and Gupta, G K and Praksh, S and Mahato, T and Chandra, S

The objective of the manuscript is to evaluate the effectiveness of NACKED EYE SINGLE TUBE RED CELL OSMOTIC FRAGILITY TEST (NESTROFT) as screening tool for detection of B-THALASSEMIA TRAIT against the HPLC method. NESTROFT and HPLC METHOD were applied to blood sample of 84 patients of suspected cases of B-Thalassemia and other haemoglobinopathies. Out of 84, Beta Thal Trait 13 cases (15.4%), Delta Beta Thal Trait 9(10.7%), Thal Major 5(5.9%), HPFH 7(8.3), Sickle Homo 12 (14.2 %), Sickle Trait 10(11.9%) Sickle Thal Trait 7(8.3%) & IDA 21(25%) cases were detected by HPLC. The NESTROFT test was successful in detecting 12/13 subjects with B-Thalassemia trait. Sensitivity of the test was 92.31 % and specificity was 63.38 %. The test was positive in detecting other haemoglobinopathies like sickle cell disease also. The test proved to be simple, cheap easy to perform and adaptable for mass screening coming close to an ideal screening test for B-Thalassemia trait.

9. **Aberrant heterosis of G-6-PD deficiency and sickle cell disorders: Need to limit family size in carrier couples in India**

   2009

   Indian Journal of Hematology and Blood Transfusion

   Balgir, R S

Background: The sickle cell disease and glucose-6-phosphate dehydrogenase (G-6-PD) enzyme deficiency are important genetic and public health challenges in India. Effect of compound heterosis of these disorders is still not fully understood and need exploration. Aims & Objectives: To study the interaction of sickle cell disease and G-6-PD deficiency in relation to reproductive outcome among some Dhelki Kharia tribal families of Orissa. Methodology: A random genetic study of screening for hemoglobinopathies and G-6-PD deficiency among Dhelki Kharia tribal community in Sundargarh district of Orissa was carried out for intervention. Out of 81 Dhelki Kharia families screened, six families with double heterozygosity for genetic anomalies were encountered. About 2-3 ml. intravenous blood samples were collected in EDTA after taking informed consent in the presence of doctor and community leaders and analyzed for hematological investigations. Analysis was carried out following the routine

standard procedures. Results: There were 12 children (about 52%) out of 23 who were either suffering from sickle cell trait or disease in concurrence with G-6-PD deficiency in hemizygous/heterozygous/homozygous condition in Dhelki Kharia tribal community of Orissa. There were on an average 3.83 number of surviving (range 2-6) children per mother in families of G-6-PD deficiency and sickle cell disorders. The average number of children (3.83) born (range 2-6 children) per mother to carrier/affected mother was much higher than the average for India (2.73). Conclusions: One of the implications of aberrant heterosis is its adverse affects on individual physiology and routine activities. To limit the family size in carrier couples to avoid aberrant heterosis in offsprings is suggested.

10. **Detection of Hb variants and hemoglobinopathies in Indian population using HPLC: Report of 2600 cases**

    2010

    Indian Journal of Pathology and Microbiology

    Sachdev, R and Dam, A R and Tyagi, G

Background: Inherited abnormalities of hemoglobin synthesis include a myriad of disorders ranging from thalassemia syndromes to structurally abnormal hemoglobin variants. Identification of these disorders is immensely important epidemiologically and aid in prevention of more serious hemoglobin disorders. Aims: High performance liquid chromatography (HPLC) forms an important tool for accurate and speedy diagnosis of various hemoglobin disorders. About 2600 cases have been studied for identification of various hemoglobin disorders in Indian population. Material and Methods: The study was performed on BIORAD VARIANT using beta thalassemia short program. Results and conclusion: Abnormal hemoglobin fractions on HPLC were seen in 327 of the 2,600 cases displayed. Of this, the beta thalassemia trait was the predominant abnormality with a total of 232 cases (8.9%). There were 15(0.6%) cases of beta thalassemia major and 16 of thalassemia intermedia. The rest comprised of Hb D Punjab (13 cases; 0.5%), Elevated Hb F (25 cases; 0.9%), Hb E (seven cases including two Hb E homozygous and five Hb E heterozygous), Double heterozygous Hb E-beta thal trait (six cases), Hb Q India (five cases), Double heterozygous Hb Q India -beta thal trait (two cases), Hb S (total cases three including one Hb S homozygous; two Hb S -beta thal trait) and one case each of Hb J Meerut, Hb D-Iran and Hb Lepore trait. Detection of this abnormal hemoglobin, particularly keeping in mind a high prevalence of Hb A2, will help in prevention of more serious hemoglobinopathies including beta thalassemia major. HPLC forms a rapid and accurate tool in early detection and management of various hemoglobin disorders.

11. **Clinical, hematological and molecular profiles of patients with sickle-cell disorders in a non-endemic North Indian Region**

    2020

    Indian Journal of Hematology and Blood Transfusion

    Yadav, D D and Hira, J K and Chhabra, S and Sreedharanunni, S and Trehan, A and Khadwal, A R and Malhotra, P and Sharma, P and Das, R

Aims & Objectives: To study the frequencies, clinico-demographic profiles and laboratory features of sickle-cell disorders (SCD) at a north Indian referral hospital with an emphasis on the role of molecular genetic analysis. Patients/Materials & Methods: All SCD patients diagnosed between January 2009 to June 2020, based on cation-exchange high pressure liquid chromatography (CE-HPLC), and confirmed by sickling test and alkaline pH electrophoresis, were included. Clinical, demographic and laboratory data including molecular findings (HbS mutation analysis by PCR-RFLP/ARMS-PCR and Î²-mutation analysis by multiplex ARMS-PCR) were collated. Results: Total 282 cases of SCD were identified: 166 sickle-cell trait, 48 sickle-cell anemia (SCA), 54 double-heterozygous sickle-b- thalassemia (Sb) and 14 double-heterozygous sickle-HbD-Punjab. Clinical, demographic and laboratory findings are summarised in Table 1. Median age at referral to our hospital was 19 and 14 years for Sb and SCA respectively. The states of Punjab and Jharkhand contributed highest numbers of Sb and SCA patients respectively. Clinically, SCA patients had more frequent pain and jaundice and slightly less frequent

splenomegaly compared to Sb group. The SCA group was more likely to have required hospitalisation and received hydroxyurea than the Sb group. Among the laboratory parameters, 29% of the SCA's had microcytosis while 12.9% had HbA2% C 3.5%. MCV<80 fl together with HbA2% C 4.0% successfully distinguished Sb and SCA (81.2% sensitivity, 96.7% specificity). However, this approach missed 18.7% (n = 9) Sb cases and mislabelled 3% (n = 1) SCA cases as Sb. On molecular testing, the predominant thalassemic allele was HBB:c.92 + 5G>C mutation (58%) followed by HBB:c.126-129delCTTT (15%), NG-000007.3:g.71609-72227del619 (6%), HBB:c.27-28insG (4%) and HBB:c.92 + 1G>T (2%). Remaining cases (n = 8, 15%) showed uncommon mutations. In one case, the RFLP pattern suggested SS-state, however, ARMS-PCR revealed the Codon 5(-CT); HBB:c.17-18delCT thalassemic mutation altering the DdeI restriction site. Amongst the Sb-group, HPLC-derived HbA0 was significantly lower (p<0.001) and HbA2 (p = 0.03) significantly higher in Sb0 in comparison to Sb + mutation groups. Discussion & Conclusion: SCD, especially Sb, is not rare in northern India. Molecular testing aids accurate characterisation of cases where parental studies are not feasible, in transfused patients, and in cases with misleading RBC indices. ARMS-PCR is superior to PCR-RFLP for the detection of HBB:c.17-18delCT mutation.

12. **Efficacy of high speed super solubility test in detection of sickle cell diseases at Rajendra institute of medical sciences, Ranchi, Jharkhand, India**

    2014

    Research Journal of Pharmaceutical, Biological and Chemical Sciences

    Prasad, C and Rai, H N and Singh, S B

Sickle cell anemia (SCA) is a genetic disorder characterized by severe hemolytic anemia and shorter life span. Diagnosis is an important aspect in the management of this disease. To assess the efficacy of Super Speed Sickle Solubility test in the diagnosis of SCA in population attending this medical institute. A total of 63 patients were screened in 2013. All the positive samples were assayed by solubility test simultaneously analysed on high-performance liquid chromatography (HPLC) 'BIO-RAD' Variant II analyzer for the confirmation along with the distinction of SCA (heterozygous) and sickle cell disease (homozygous). Out of all 63 patients screened, 29 were found to be positive with HPLC as well as with solubility test too. A total of 10 samples was diagnosed as SCA (heterozygous), 12 samples were diagnosed as sickle cell homozygous and 7 cases as Sickle Thal with HPLC and Solubility tests. In case of Sickle cell Homozygous, Solubility test was found to be fairly effective with 75.0 % and 80.85% sensitivity and specificity respectively, with the predictive value of positive test 57.14% and a predictive value of negative test 90.47 % along with an Accuracy of 79.37 %. It was observed that in case of Sickle Cell Trait, the sensitivity specificity, positive predictive and negative predictive values were 76.92 %, 97.5 %, 57.14% and 92.8% respectively. We found that Solubility test in Sickle Thal Trait revealed sensitivity of 70.0 %, specificity 73.58 %, positive predictive value 33.33 %, negative predictive value 92.85 % along with an Accuracy of 73.0 %. This study concludes that solubility test is better for mass screening and does not need any microscope. It is also cost effective test for early detection of disease and for timely intervention to minimize morbidity and mortility.

13. **Newborn screening for sickle cell disease in a tribal area of south Gujarat, India**

    2011

    American Journal of Hematology

    Italia, Y M and Colah, R B and Ghosh, K K and Rajwadi, H P and Mehta, V I and Raicha, B K and Parmar, A N and Desai, T O and Italia, K Y and Dongre, I and Khatri, R and Krishnamurti, L

Background: Newborn screening (NBS) and enrollment in comprehensive care for patients with sickle cell disease (SCD) has dramatically improved survival and disease outcomes. NBS has mainly been implemented in structured health care systems in western countries. There are infrastructural barriers to implementation of NBS in developing countries. This is further complicated when, as is the case in India, SCD disproportionately affects communities that suffer extreme socio-economic disadvantage and physical and cultural isolation. SCD is a major

public health problem facing these disadvantaged indigenous communities also known as Adivasi or Scheduled Tribes. There is a need for developing NBS and comprehensive care for SCD specifically targeting these communities. Aims: To determine the feasibility of NBS for sickle cell disease, education, counseling and comprehensive care targeting tribal populations in Gujarat, India. Methods: Valsad Raktadan Kendra has been conducting community based screening in south Gujarat since 1984 and has been the nodal agency for the state sickle cell program since 2006. The program is integrated into the state run medical and health system which extends to down to the Primary health center (PHC) that provides primary health care at the Development Block, the smallest administrative unit of the state. Mulitpurpose health workers take care to the doorstep of the family. Starting in 2008 we piloted implementation of NBS, counseling and comprehensive care in four districts of south Gujarat. After parental education about SCD, blood was collected from newborns by heel stick at birth center or home. Filter paper was mailed to the laboratory at Valsad Raktadan Kendra and analysis carried out by HPLC (VARIANTnbs newborn hemoglobin screening and sickle cell program, Bio-Rad Laboratories Inc). Confirmatory testing was performed by isoelectric focusing and molecular methods at National Institute of Immunohematology, Mumbai. Result: Of the 3059 newborns tested 27 infants were detected to have SCD, 374 were detected to have sickle trait and 2658 were normal. All babies with an abnormal screen were located. All infants with SCD were enrolled in comprehensive care. The families of infants with sickle cell trait received genetic counseling. All pre-analytical, analytical and post-analytical systems have been quality tested and standardized. Program Evaluation using the NBS program evaluation and assessment scheme (Therrell, B et al Semin Perinatol 2010) is currently under way. NBS is now being extended to 12 districts with a total tribal population of over 6 million. Conclusion: Newborn screening, counseling and comprehensive care for SCD targeting an extremely disadvantaged population in a developing country is feasible.

14. Transcranial doppler screening in children with sickle cell anemia is feasible in central india and reveals high risk of stroke

2019

Blood

Jain, D and Ganesan, K and Sahota, S and Darbari, D S and Krishnamurti, L and Kirkham, F J

Introduction: India has been identified as having the second largest number of births with sickle cell anemia (SCA) in the world after Africa, with estimated 44,400 new-borns affected per year. SCD was previously reported to have a milder course in children from India, with less severe disease among aboriginal tribal populations than in non-tribal populations. Recent reports indicate the occurrence of severe manifestations of SCD in both tribal and non-tribal populations in India. Stroke is one of the serious complications of SCD, but there are no data on transcranial Doppler (TCD) screening for evaluating children with SCD in India who may be at high risk for strokes. The objective of this study was to assess the feasibility of using TCD to measure time averaged maximum of the mean velocities (TAMMV) in the intracranial arteries in children attending a tertiary centre in central India. Methods: STUDY DESIGN: A cross sectional study was conducted in consecutively recruited stable children of either sex with homozygous SCA proven by electrophoresis and high performance liquid chromatography in the age group of 1-26 years. Patients who were febrile, acutely ill, hypoxic or asleep were not included in the study as these conditions can falsely elevate the intracranial blood flow velocities. Patients with hemoglobinopathies other than HbSS or S/b0 Thalassemia and those with a history of congenital neurological illness were excluded. DETERMINATION OF TCD VELOCITY: TCD was performed in a tertiary care center in Nagpur using either an imaging machine (Lasiq s8) in the department of radiology or a portable non-imaging TCD (Compumedics); for both a probe of frequency 2Mhz was used. Maximum values for TAMMV in the Middle (MCA) and Anterior (ACA) cerebral arteries were measured in all; for the non-imaging TCD values for posterior cerebral artery (PCA) and basilar artery were also obtained. The results of the first scan performed on these individuals were included in this study. Using values similar to the STOP trial, TAMMV of each of these vessels were categorized as follows: Normal <= 170cm/s; Conditional-between 170 and 199 cm/s; Abnormal >= 200 cm/s; Low <50 cm/s and unobtainable. MEASUREMENT OF HAEMATOLOGICAL VALUES: Laboratory parameters such as

Hemoglobin, white blood cell count (WBC), Mean corpuscular volume (MCV) and hemoglobin F (HbF) levels of the patients in the study were also included if the parameters were available on the day of TCD or within 90 days of TCD study. MEASUREMENT OF HEIGHT, WEIGHT AND BMI: The height and weight of each of the patients on the day of TCD or within a period of 60 days from the TCD were measured and the body mass index (BMI) was calculated. Results One hundred and twenty children and youth aged 1-26 (median 7) years, 67 male (56%), were recruited. Of the 120 patients, 106 (88.5%) belonged to the Scheduled Caste category, 3 (2.5%) to the Scheduled Tribe category and 11 (9.1%) to the Other Classes category. Three (2.5%) had had a clinical stroke and 8 (7%) had had seizures, one of whom also had a stroke. Twenty-seven (23%) children had TAMMV outside the normal range. Five had abnormal TAMMV in the MCA (n=4) and/or ACA (n=1), 8 had conditional TAMMV in the MCA (n=7) and/or ACA (n=1) while 14 patients had low (n=12) or unobtainable (n=2) TAMMV in the MCA. One child with stroke had low TAMMV and one had conditional TAMMV while the third had normal TAMMV. Of the 7 with isolated seizures, one had low TAMMV and one had conditional TAMMV while the remaining 5 were normal. BMI was 8.6-25.3 (median 14.1), height/weight was 3.4-10.3 (median 6.5), hemoglobin was 43-134 (median 81) g/L, oxygen saturation 87-100 (median 99)%, HbF was 1.9-60 (median 21) g/dL, MCV was 59.1-96.7 (median 83.2) fl, WBC was 2.3-35.9 (median 10.1)âˆ—109. Those with TAMMV outside the normal range were not different from those with normal TAMMV in terms of age, BMI, Height/weight, or recent hemoglobin, oxygen saturation, HbF, MCV, or WBC. Discussion This study demonstrates the feasibility and importance of TCD screening in Indian SCD population. TAMMV on TCD was outside the normal range in nearly a quarter of children with SCD, as has been reported in studies in other populations. The findings of this study may not be representative of stroke risk in tribal populations since they were underrepresented in this study. These data provide the rationale for implementing systematic screening with TCD to reduce the risk of stroke in children affected by SCD in India.

15. **Diagnosis of a novel hemoglobinopathy of compound heterozygosity of hemoglobin S/hemoglobin Q India**

    2014

    Indian Journal of Hematology and Blood Transfusion

    Sakhare, S and Parab, S and Sengupta, C and Velumani, A

Summary: Thalassemia is a quantitative genetic disorder resulting due to mutations in the globin genes of hemoglobin. Double heterozygosity of HbS with various other hemoglobinopathy (like Hb E, HbD Punjab and Hb C) is already reported. However HbS along with HbQ India is still not reported in literature. Introduction: A novel double heterozygosity for the alpha chain variant Hb Q India and beta chain variant Hb S is described. Hb S is prevalent in central part of India while Hb Q India in its heterozygous state is found mainly in Sindhi families. Materials and Methods: Identification of both the variants, Hb S and Hb Q India was done based on chromatograms of HPLC (Tosoh G8 HPLC analyser, Japan) and capillary zone electrophoresis (CE, Capillarys 2 Flex piercing, Sebia, France). Confirmation of variants was done by PCR based amplification refractory mutation system (ARMS) technique. Results: Both HPLC and CE confirmed presence of Hb S. HPLC showed a pointed narrow peak of Hb Q India at retention time of 4.55-4.56 min while it is eluted in Hb D zone on CE. A hybrid variant of this alpha and beta globin chain was eluted in Hb C window and Hb C zone on HPLC and CE, respectively. Molecular studies using ARMS technique confirmed these findings. Both the cases showed positive sickling test and presented with mild anemia. Conclusion: We are presenting for the first time two index cases for compound heterozygosity of Hb S with Hb Q India.

16. **Evaluation of Paper-Based Point of Care Screening Test for Sickle Cell Disease**

    2021

    Indian Journal of Clinical Biochemistry

    Kumar, R and Mishra, S and Gwal, A and Shanmugam, R

The aim of the study is to evaluate the stability and longevity of the paper-based screening test for the sickle cell disease in relation to different temperatures and storage time. Blood stain patterns were interpreted after spotting the blood-buffer mixture (phosphate buffer, saponin and sodium metabisulfite) on chromatographic paper (Whatman no. 3). The stability of the buffer was tested after keeping the buffer at different temperature for 24Â h. Longevity of the buffer was tested post storage for various time intervals. Test indicated reproducibility with the buffer stored at 4Â°C. The 15% metabisulfite buffer was found to be stable up to 180Â days at 4Â°C and showed accurate identification of all genotypes. The tests revealed 100% sensitivity and 100% specificity in identification of HbS. However, the sensitivity of differentiation between sickle cell trait (AS) with disease (SS) was found to be 97.7% with 100% specificity. The paper-based screening test may be used as a method of choice for the screening of sickle cell anemia in community-based screening programs. The low-cost, rapid, and accurate point of care testing tools offer an avenue for effective screening in developing nations.

17. **Screening of Dry Blood Spots from Newborns by Two High Performance Liquid Chromatography (HPLC) Systems: A Comparison of Their Ability to Diagnose Both Sickle and Non-sickle Hemoglobinopathies**

    2021

    Indian Journal of Hematology and Blood Transfusion

    Ramani Daruwalla, M and Das Gupta, A and Pawar, R

Screening of newborns for the presence of sickle hemoglobin (HbS) is aimed at reducing the morbidity and mortality associated with sickle cell disease in early childhood. The high cost and limited availability of dedicated high performance liquid chromatography (HPLC) systems specially designed for screening of dry blood spots (DBS), however, restrict a wider application of this preventive approach. Therefore, we examined the ability of a commonly used HPLC system for detection of hemoglobinopathies in DBS samples in order to find an alternative for the dedicated newborn screening (NBS) HPLC system. DBS samples from 7522 newborns were first examined by Variant NBS HPLC system (Bio Rad, USA) for the presence of hemoglobinopathies. Positive samples were then analysed by Variant II system (Bio Rad, USA), another platform commonly used for hemoglobinopathy screening of anticoagulated blood samples. Eighty six newborns (1.1%) showed the presence of hemoglobinopathies (HbS 28, HbE 21, HbD 27, HbQ India 9 and Hb Barts 1) by Variant NBS systemâ€"all in heterozygous state. There was 100% correlation between the two sets of results obtained by the two HPLC systems. Newborns with HbQ India showed an additional Hb peak in HPLC resulting from combination of the abnormal alpha globin chain of HbQ India with the normal gamma chain of HbFâ€“â€˜HbF Q Indiaâ€™. Variant II HPLC system, used for routine hemoglobinopathy screening in anticoagulated blood, can also be used for screening DBS samples. This obviates the need for a dedicated NBS system for hemoglobinopathy screening in newborns. We also demonstrated that both the systems are equally competent in detecting non-sickle Hb variants in DBS samples.

18. **Sonographic screening for abdominal organ involvement in sickle cell anemia-a step towards better patient care**

    2017

    Journal of Krishna Institute of Medical Sciences University

    Lakhkar, B B and Lakhkar, B N and Lakhkar, B B

Background: Sickle cell disease is characterized by repeated crisis and need for frequent transfusions. Abdominal crisis are common and potentially can damage any abdominal organ. Screening for organ involvement will lead to early detection and better patient care. Aim and Objectives: To see whether ultrasound can be a better noninvasive technique for early detection of organ involvement. Material and Methods: Prospective cross sectional observational study done on patients admitted in pediatric ward of a medical college. Total of 150 patients, already diagnosed to have sickle cell anemia (homozygous 110 and heterozygous 40) was included in the study. All the patients were in steady state. Demographic, clinical biochemical details were noted and were subjected to ultrasonography. Renal artery, Being end artery, Doppler study was also done. All the modalities were compared for early detection. Results: Majority of patients (77%) were between 1 to 30 years with male

female ratio of 2:1. Recurrent fever (64%) and recurrent abdominal pain (47%) were most common symptoms and anemia (66%), hepatomegaly (62%), splenomegaly (21%) were most common signs. When clinical examination, biochemical tests and ultrasonography were compared for organ detection, ultrasound significantly detected more patients (p=<0.05). Ultrasonography of kidney included renal doppler also. Renal involvement by microalbuminuria measurement was of same as ultrasonography. Organ involvement increased with age. Conclusion: Ultrasonography was good noninvasive technique for organ detection but kidneys yield was better with Doppler study. Most common organ found to be affected was liver. Involvement increased with age. Early detection helps clinicians to avoid drugs toxic to involved organs.

19. **Common Hb variants encountered in HbA1C measurements on routine diabetic backup**

    2016

    Indian Journal of Clinical Biochemistry

    Iswarya, J and Job, V

Introduction: Glycated Hb is used routinely to monitor long-Term glycemic control in people with diabetes mellitus, as it is related directly to risks for diabetic complications. The higher the glycated hemoglobin, the poor will be the glycemic control. The accuracy of HbAlc methods can be affected adversely by the presence of hemoglobin (Hb) variants or elevated levels of fetal hemoglobin (HbF).The most common Hb variants found worldwide are HbS, HbE, HbC and HbD. To avoid reporting of inaccurate results due to the interferences from these variants, ion-exchange chromatogram should be carefully examined. This study is focused on the investigation of abnormal/abberant peaks in the chromatogram. Aim: To check the presence of Hb variants in the measurement of HbAlC in routine diabetic workup patients and its effect on reportability. Materials: 7120 whole blood samples from patients of Christian Medical College, Vellore. Method: Samples were analyzed using Ion-exchange High pressure liquid chromatography (variant II turbo HbAlC kit) Results: HbAlC values of 7120 samples measured over a one month period was analysed. 164 (2.3%) showed variants. HbS and Hb C - 12.1%, HbD and Hb E - 70.1%, Hb F together with the other variants - 7.9%, Elevated Hb F alone was found to be 3.0%, No peaks in the chromatogram - 4.26% , P3&P4 peaks -2.43%. Conclusion: No significant interferences were seen in HbAlC measurement due to the variants HbS, HbD, HbC, HbE since the concentrations were < 40%, so values were reportable. HbF concentration of > 25%, HbAlC was not reportable. P3 & P4 peaks of >10%, HbAlC could not be reported. In 9.69 % of cases of the variants, the HbAlC values could not be reported and alternate separation methods need to be used. Only 0.2% of the total number could not be reported in this group.

20. **Near extinction of HbS among the tribes in Bengal: An effect of epistasis?**

    2017

    Blood

    Ray, R and Roy, S and Sarkar, A and Chowdhury, R and Bhattacharyya, M

Introduction : Tribal communities are genetically isolated populations mostly following endogamy. The large tribal population in India inhabits widely varying ecological and geo-climatic conditions in different concentration throughout the country. It is widely established that the high frequencies of genetic blood disorders (haemoglobinopathies) are the result of evolutionary selection (Haldane 1949; Flint et al. 1998). The sickle gene, which protects against malaria, provides an example of balanced polymorphism (Stuart M.J; 2004). The tribal area in India is mostly associated with high incidence of malaria. Thalassaemia is highly prevalent among the tribal communities in india; and interestingly the occurrence rate of a particular mutation/ type of thalassaemia varies to a great extent from one to another (R.Colah, 2014 ; R.Dastidar, 2007). According to a survey by ICMR the Sickle Cell gene was found amongst different tribal groups of India; which varies from 5 to 34 % (M.Kaur; 2013). The prevalence of alpha thalassaemia, which also gives protection against malaria, varies throughout the country. The frequency and distribution of thalassaemia among the tribes India is less well-documented; especially in the eastern part of the country where there have not been much thorough studies upon hemoglobinopathies among the tribes with a large number sample population. In this study the primary aim was to investigate the

prevalence of anemia, Sickle Cell disease and other mutant hemoglobin amongst the tribal community in west Bengal. Method: Over a duration of 18 months, 17,369 school going children (age= 10-18 years), among the tribal community, from almost all the districts of West Bengal were included in this study; and were initially screened by complete haemogram and HPLC analysis. Detection for alpha 3.7 deletion & alpha 4.2 deletion, the most common form of alpha gene defect in India, were carried by GAP-PCR; and HbS mutation analysis by ARMS PCR. Result: Approximately 6 % among the total study population was found to be carrier for beta thalassaemia; and only 0.4 % of the total population with HbS. 30 % of the population were found to be absolute normal based on the HPLC parameters and RBC indices [Table-1,2 & 3; Figure 1] . Around 62% were found to have 'normal HPLC values with abnormal RBC indices' who were subjected to 'further investigation'. For 'further investigation' we initially selected six districts; under which total number of individual screened were 5357; among which 65% were found to have 'normal HPLC values with abnormal RBC indices' after initial routine screening [Table-4, 5,] who were subjected to further investigation for the detection of alpha 3.7 deletion and alpha 4.2 deletion. Almost 83% of them were found to carry (3.7 or 4.2 or both 3.7 + 4.2) alpha gene deletion [Table 6, 7, 8]. Though prevalence of alpha thalassaemia carrier was found to be high; HbS carrier was found to be only 0.3% by HPLC. The samples carrying alpha deletion were re-checked for the presence of HbS mutation; none of the which was found carry silent / suppressed form of HbS mutation. Discussion : Recently few studies have focused on understanding the co-association between alpha gene mutation and HbS in populations under constant pressure of malaria; which have shed light upon few aspects like-Negative Epistasis, Genetic Drift, Positive Selection etc regulating the outcome (S. Penman,2011; MB Rumaney, 2014). The high prevalence of alpha gene mutation found in our study may be attributed to the fact that alpha mutation is also known to have protective role against malaria. At the same time there is a genetic drift which has caused lowering the prevalence of HbS. The widely varying prevalence of alpha deletion (high) and exceptionally low prevalence of HbS (exceptionally low) may be a consequence of epistasis and positive selection depending upon the risk factors associated with the mutations of two distinct alleles; which can be described by mathematical modeling (S. Penman;2011). Conclusion: Though asymptomatic, such high prevalence of alpha gene mutation is alarming as it may result in high occurrence of HbH disease among the tribal population where there is high rate consanguine marriage; if not intervened through proper marriage counseling and raising general awareness in the society (Figure presented).

21. **Computer vision and deep learning assisted microchip electrophoresis for integrated anemia and sickle cell disease screening**

    2020

    Blood

    An, R and Man, Y and Iram, S and Kucukal, E and Hasan, M N and Solis-Fuentes, A and Bode, A and Hill, A and Cheng, K and Huang, Y and Ahuja, S and Little, J A and Hinczewski, M and Gurkan, U A

Introduction: Anemia affects a third of the world's population with the heaviest burden borne by women and children. Anemia leads to preventable impaired development in children, as well as high morbidity and early mortality among sufferers. Inherited hemoglobin (Hb) disorders, such as sickle cell disease (SCD), are associated with chronic hemolytic anemia causing high morbidity and mortality. Anemia and SCD are inherently associated and are both prevalent in the same regions of the world including sub-Saharan Africa, India, and south-east Asia. Anemia and SCD-related complications can be mitigated by screening, early diagnosis followed by timely intervention. Anemia treatment depends on the accurate characterization of the cause, such as inherited Hb disorders. Meanwhile, Hb disorders or SCD treatments, such as hydroxyurea therapy, requires close monitoring of blood Hb level and the patient's anemia status over time. As a result, it is crucially important to perform integrated detection and monitoring of blood Hb level, anemia status, and Hb variants, especially in areas where anemia and inherited Hb disorders are the most prevalent. Blood Hb level (in g/dL) is used as the main indicator of anemia, while the presence of Hb variants (e.g., sickle Hb or HbS) in blood is the primary indicator of an inherited disorder. The current clinical standards for anemia testing and Hb variant identification are complete blood count (CBC) and High-Performance Liquid Chromatography (HPLC), respectively. State-of-the-art laboratory infrastructure and trained personnel are required for these laboratory tests. However, these resources are typically scarce in low- and middle-income countries, where anemia and Hb disorders are the most prevalent.

As a result, there is a dire need for high accuracy portable point-of-care (POC) devices to perform integrated anemia and Hb variant tests with affordable cost and high throughput. Methods: In 2019, the World Health Organization (WHO) listed Hb electrophoresis as an essential in vitro diagnostic (IVD) technology for diagnosing SCD and sickle cell trait. We have leveraged the common Hb electrophoresis method and developed a POC microchip electrophoresis test, Hemoglobin Variant/Anemia (HbVA). This technology is being commercialized under the product name â€œGazelleâ€ by Hemex Health Inc. for Hb variant identification with integrated anemia detection (Fig. 1A&B). We hypothesized that computer vision and deep learning will enhance the accuracy and reproducibility of blood Hb level prediction and anemia detection in cellulose acetate based Hb electrophoresis, which is a clinical standard test for Hb variant screening and diagnosis worldwide (Fig. 1C). To test this hypothesis, we integrated, for the first time, a new, computer vision and artificial neural network (ANN) based deep learning imaging and data analysis algorithm, to Hb electrophoresis. Here, we show the feasibility of this new, computer vision and deep learning enabled diagnostic approach via testing of 46 subjects, including individuals with anemia and homozygous (HbSS) or heterozygous (HbSC or S(3-thalassemia) SCD. Results and Discussion: HbVA computer vision tracked the electrophoresis process real-time and the deep learning neural network algorithm determined Hb levels which demonstrated significant correlation with a Pearson Correlation Coefficient of 0.95 compared to the results of reference standard CBC (Fig.1D). Furthermore, HbVA demonstrated high reproducibly with a mean absolute error of 0.55 g/dL and a bias of -0.10 g/dL (95% limits of agreement: 1.5 g/dL) according to Bland- Altman analysis (Fig. 1E). Anemia determination was achieved with 100% sensitivity and 92.3% specificity with a receiver operating characteristic area under the curve (AUC) of 0.99 (Fig. 1F). Within the same test, subjects with SCD were identified with 100% sensitivity and specificity (Fig. 1G). Overall, the results suggested that computer vision and deep learning methods can be used to extract new information from Hb electrophoresis, enabling, for the first time, reproducible, accurate, (Figure Presnted) Figure 1: Computer vision and deep learning assisted microchip electrophoresis for integrated anemia 3 r d sickle cell disease Screening. (A-B) Peim-of-Care (POC) Hemoglobin Variant/Anemia (HbVA) diagnostic system is composed of a single use plastic microchip electrophoresis cartridge and an affordable portable robust reader. (C) Blood sample and a standard calibrator is mixed at a lined ratio arid applied inlo the cartridge. Total hemoglobin (Hb) separates within <2.5 minutes while individual Hb variants further separate between 2.5 to S minutes. Tbe erectromigraiion pattern of tolai Hb, standard calibrator is recognized by trained artificial neural network (ANN) based deep learning system to determine Hb level and detect anemia. (D} HbVA Hb level measurement displayed a significant correlation wiih clinical standard CBC (Pearson correlation coeftioienl: 0.95. p<0.001). (E) HbVA level measurement demonstrated high raproducibJy Willi a mean absolute error of 0.55 gfdL and a bi as of -0.10 gj'dL (95% Ii rn its of agreement: 1.5 g/dL} according to Bland-Altrnan analysis. (F) HbVA anemia detection achieved 100% sensitivity and 92.3% specificity with a receiver operating characteristic area under the curve [AUC} of 0.99. (G) HbVA demonstrated 100% sensitivity and specificity in identifying individuals with homozygous (HbSS) and heterozygous (HbSC) SCD among I h e 4 6 subjccls tested, within the same tesl.

22. A study of pulmonary function tests in sickle cell anaemia patients in Raipur District, Chhattisgarh, India

2015

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Singh, K

The inherited disorders of haemoglobin are the commonest single gene disorder of the world population. Sickle cell anaemia being the most widespread and numerically the most important haemoglobinopathy in the world today The major features of sickle cell disease (SCD) in most patients are life-long anaemia and the consequences of recurrent vaso-occlusion. Many complications of SCD involve anaemia, vaso-occlusion etc. Impairment of pulmonary function is a common complication of SCD. The patients suffering from this disease frequently present with complaints referable to the pulmonary system although other systems are also involved. Hence present study was carried out to evaluate the pulmonary function tests in sickle cell disease patients (HbSS),sickle cell trait patients(Hb AS) with normal person (HbAA) non-sicklers.1) To study the pulmonary alterations in cases of homozygous SS & heterozygous AS Sickle Cell Disorder subjects.2) To compare the parameters with normal

healthy controls & assess the importance of PFT in "Steady State"(free from complications or crisis)as an objective evidence to predict the risk of "Sickle Cell Chronic Lung Disease" in future. A cross sectional study was done in 50 cases of SCD (22HbSS & 28HbAS) and age and sex matched normal 50 HbAA controls. From the various measured pulmonary function test(PFT)parameters Forced Vital Capacity(FVC),Forced Expiratory Volume in 1 sec(FEV1),FEV1/FVC, Forced Mid Expiratory Flow(FEF25%-75%) were selected for the study. The data collected was subjected to statistical analysis involving computation of Mean, Standard deviation, Independent T test. Mean value of FVC, FEV1, FEV1/FVC and FEF25%-75% were found to be significantly lower than normal controls, but the difference in FVC between HbAS and HbSS turned out to be statistically non-significant whereas the difference in FEV1, FEV1/FVC,FEF25%-75% between HbAS and HbSS was statistically significant. There were significant reductions in pulmonary function test parameters in sickle cell anaemia patients as compared to normal controls indicative of mixed pattern (both restrictive and obstructive) lung impairment in sickle cell anaemia.

23. Evaluation of a rapid and cost effective POCD for screening sickle cell disease in Indian population

2019

Indian Journal of Hematology and Blood Transfusion

Ranjan, R and Pandey, H and Sharma, A and Lata, S and Kishor, K and Tyagi, S and Seth, T and Mahapatra, M and Saxena, R

Aims & Objectives: Sickle cell disease is one of the most common single- gene disorders in the Indian population.>312,000 births are affected annually by sickle cell anaemia (SCA). Early interventions such as newborn screening, penicillin prophylaxis and hydroxyurea can substantially reduce the mortality and morbidity associated with SCD. Nevertheless, their implementation in Asian countries has been mostly limited to pilot projects. Recent development of low-cost point-of-care testing (POCT) devices for sickle haemoglobin (HbS) could greatly facilitate the diagnosis of those affected. Patients/Materials & Methods: We conducted the real-world assessment of a low-cost POCT device, HemoTypeSC, in Indian Sickle Cell Disease Patients families. The study involved parallel testing of 50 known cases of Sickle Cell Disease family individuals by using Point of Care device and HPLC between January to June 2019. The discordant samples were analysed by molecular diagnosis. Results: We found that, in optimal field conditions, the sensitivity, specificity, Positive Predictive value (PPV), Negative predictive value (NPV) of the test for SCD were 97.5%, 100%, 100%, 90.9%, respectively. It suggests that HPLC results might not be as useful and cost effective in a resource-poor setting as usually considered. Discussion & Conclusion: The use of such a POCT device can be scaled up and routinely used across multiple healthcare centres in India, which would offer great potential for the identification and management of vast numbers of individuals affected by SCD who are currently undiagnosed.

24. Efficacy of solubility test in screening of sickle cell diseases: A tertiary care centre based study

2020

Indian Journal of Hematology and Blood Transfusion

Chandpara, K P and Patel, M M and Tilala, A and Sanghani, R

Aims & Objectives: To find out specificity and sensitivity of solubility test in screening of sickle cell disease at tertiary care center, Surat. Patients/Materials & Methods: A cross-sectional observational study was carried out at tertiary care centre, Surat. A total of 983 samples were studied over a period of 1 year. All the samples were subjected to solubility test and were further analysed on HPLC BIORAD analyzer for confirmation along with the distinction of Sickle cell trait and Sickle cell disease. Results: Out of 983 samples screened, 684 samples were found to be positive with the solubility test and 299 samples were solubility negative. Out of 684 solubility positive samples, 481 were diagnosed as sickle cell trait (heterozygous), 200 were diagnosed as Sickle Cell Disease (homozygous), 1 was diagnosed as Sickle cell- HbD disease and 2 were normal on HPLC. Out of 299 solubility

negative samples, none showed Sickle cell disease or trait or any other sickle cell variants. on HPLC. We calculated sensitivity of 100%. Specificity was 99.3%, positive predictive value was 99.7% and negative predictive value was 100%. Discussion & Conclusion: Solubility test is very effective as screening test due to high specificity and sensitivity. Though solubility test is very cheap, it cannot differentiate between Sickle Cell Trait and Sickle Cell Disease hence, confirmation is to be done by electrophoresis or HPLC.

25. **Assessment of knowledge and premarital screening regarding sickle cell disease among adults**

    2021

    Journal of Clinical and Diagnostic Research

    Sakharwade, P T and Joshi, V D

Introduction: Sickle Cell Disease (SCD) is the disorder of the blood having tendency to get transferred from one generation to the next generation. Sickle cell disorder may be avoided if people become conscious of their carrier status and can do so by enhancing awareness and undertaking pre-marital screening. Understanding that even the Government of India promotes premarital screening of SCD before marriage. Aim: To assess the knowledge and screening regarding SCD among unmarried adult. Materials and Methods: An analytical research study with a cross-sectional research design was used. A total of 40 unmarried adults including male and female were participated in the study from November 2019 to December 2019. The samples were selected using purposive sampling technique and structured questionnaire was used for data collection and sickling test was used for premarital screening. Results: Most of the unmarried adults had average (40% subject) and good (42.5% subject) level of knowledge (Mean score 9.10Â±3.07) and for SCD, 18% of adults had positive premarital screening results. There was significant association of knowledge score in relation to education (p-value 0.02) and caste (p-value 0.047) of the adults. Conclusion: The study concluded that considering seriousness of SCD it is needed to get control over SCD and prevent transfer of it from one generation to next generation through public education, screening of SCD and other preventive measures.

26. **Hemechip: A portable, affordable point-of-care diagnostic technology for detecting hemoglobin disorders**

    2018

    American Journal of Tropical Medicine and Hygiene

    Gurkan, U A and Hasan, M N and Fraiwan, A and Thota, P and Galen, P

Genetically inherited hemoglobin (Hb) disorders are of global public health concern. There are more than 700 hemoglobin disorders: HbS, HbC, and HbE are the most widespread Hb variants. HbS and HbC are associated with sickle cell disease. Sickle Cell Disease (SCD) affects between 300,000 to 400,000 newborns every year, and more than 75% of these infants are born in sub-Saharan Africa and India. Of these, WHO estimates that between 50-80% die before reaching age 5. Both the World Health Assembly and the United Nations recognize SCD as a public health priority and have called on countries to tackle the disease. HbE, another structural hemoglobin variant, occurs widely throughout the eastern half of the Indian subcontinent, Bangladesh, Myanmar, and east and southeast Asia. The current clinical standards for diagnostic testing, such as High Performance Liquid Chromatography (HPLC), are associated with high cost per test as well as high cost of infrastructure. Moreover, these clinical standards require centralized laboratories, resulting in delayed turnaround times (several weeks in some regions) and logistical complexities. The geographical regions prevalent with these Hb disorders include some of the lowest-resourced countries in the world, and therefore, early diagnosis of hemoglobin disorders remains a challenge. To address this need, we developed HemeChip, a mass-producible, low-cost version of electrophoresis on a microchip, able to detect and quantify these Hb variants. HemeChip is a robust, highly reliable point-of-care technology that can separate, detect and quantify Hb variants in blood. This rapid (<10 minutes) and easy-to-use test can be performed by minimally trained personnel using only a finger-prick volume of blood. HemeChip can categorize a blood sample as Normal (HbAA), Sickle Cell Trait (HbAS), Sickle Cell Anemia (HbSS), Hemoglobin SC disease (HbSC), and HbE variants. In preliminary tests, with a sample size of 122 (42

HbAA, 36 HbAS, 34 HbSS, and 10 HbSC), HemeChip yielded a high accuracy (> 96%) compared to standard laboratory tests.

27. Community based screening and management of adolescent anemia in tribal areas of India key to reduction in maternal mortality

2011

Journal of Adolescent Health

Joshi, A and Foundation, D

Purpose: Prevention of anemia amongst adolescent girls has a great potential in reducing the risk of maternal death. More than half of young adolescents in Gujarat State of India, are anemic and its prevalence is considerably higher among those in (74%). While many school and clinic based interventions have shown promising results, albeit with poor scalability and replicability, community based interventions within the existing government delivery system are scarce. Methods: Deepak Foundation, a voluntary agency initiated screening of young mothers for anemia to promote compliance for consumption of iron and folic acid (IFA) supplement and referral of severely anemic mothers at tertiary care facilities. The Foundation is implementing anemia control program (ACP) as part of a larger intervention Safe Motherhood and Child Survival project covering 700,000 tribal populations in the district in partnership with the Government of Gujarat. The ACP leverages on monthly nutrition and health days (NHD) campaigns held in all village jointly by the Department of Health and Family Welfare and Women and Child Development to provide preventive, promotive, and curative health and nutrition services to women and children. The joint initiative is conducted with active involvement of village based committees Apart from conducting blood and urine test, information on prevention and control of anemia by demonstration of recipes made locally available, culturally acceptable, iron rich ingredients, distribution of IFA and deworming tablets, and identification of severely anemic girls, their counseling and referral to equipped health centers are also facilitated through the campaign based approach of the intervention. Each beneficiary is provided with a color-coded card specifying the blood group, Hb and glucose level to motivate him or her to comply with appropriate treatment. Results: A total of 322 campaigns were conducted during a period of 7 months (i.e., January-July 2010) in which 1810 adolescent girls were covered. Screening for anemia showed that nearly 95.3% of these girls were anemic (Hb <12 g/dL), 53.6 % were moderately anemic (Hb 7-9.9 g/dL) and 2.2 % were severely anemic (Hb <7 g/dL). IFA tablets through the Government's stock were distributed to 81.7% girls and deworming to 4% girls. A total of 42.5% of severely anemic girls were able to access appropriate treatment (double IFA supplements, blood transfusion, intra-venous injectable iron) at equipped health facilities. As early marriage (before 18 years) is common in these areas, as many as 9.6% of these adolescent girls were pregnant and 12.3% were nursing, indicating much higher iron requirements over and above that required for their own growth. Conclusions: The prevalence of anemia was disproportionately high among tribal women due to poverty, inadequate diet, prevalence of sickle cell anemia, tapeworm infestation, malaria, physiological conditions pregnancy and lactation, and poor access to health services. Factors such as timely screening of young women for anemia, compliance to intake of iron supplements and the correct estimates on prevalence of the problem are imperative to design appropriate and intensive intervention strategy for curtailing anemia among young women who die needlessly during pregnancy and postpartum period in tribal areas.

28. Study of hemoglobinopathies in Ajmer Region (Rajasthan)

2016

Indian Journal of Hematology and Blood Transfusion

Pachori, G and Toor, S S and Kasliwal, N and Sharma, R

Introduction and Background: Hemoglobinopathy is an inherited condition with alteration in the structure or quantity of hemoglobin, which reduces the oxygen carrying capacity of blood, manifesting as anemia that is unresponsive to conventional iron therapy. Patient/ Material and Methods: Data of 190 patients was collected for 6 months, retrospectively, who were screened by using High Performance Liquid Chromatography, HPLC (Bio

Rad Variant II), red cell indices, peripheral blood film (PBF) and sickle cell test. Patients with severe anemia were included in the study. Results: A total of 44 (23.15 %) cases of various abnormal hemoglobins were detected using combination of red cell indices and HPLC technique. Most common hemoglobinopathy detected was 26 (13.68 %) cases of Î²-thalassemia minor, 7 (3.68 %) cases of delta-beta thalassemia, 5 (2.63 %) cases of Î²-thalassemia major, 2 (1.05 %) cases each of homozygous hemoglobin-D disease and hemoglobin-Q disease, 1 (0.52 %) case each of hemoglobin E disease and HbS-beta thalassemia. Out of total cases detected, 23 (52.27 %) cases were female patients, and 21 (47.72 %) cases were males. The age group of patients ranged from 6 months to 80 years, with most cases of bthalassemia minor detected under 5 years of age. Conclusions: HPLC is an accurate and reliable tool to screen patients for hemoglobinopathies, especially targeting patients with refractory anemia. Screening and identification of these conditions has special importance in our national goal of achieving 12 gm% hemoglobin by the age of 12 in all children in the country.

29. **Detection of hemoglobinopathies in new born screening (NBS): An experience at a reference laboratory**

    2014

    Indian Journal of Hematology and Blood Transfusion

    Mehrotra, V and Chaudhari, P and Gupta, N and Salvi, S and Ramani, M and Gupta, A D

Introduction: Diagnosis of sickle cell disease prior 4 months of life allows early administration of penicillin prophylaxis with resultant decrease in morbidity and mortality. Hemoglobin analysis of eluates from dry blood spots (DBS) by high-performance liquid chromatography (HPLC) permits centralized testing of new-born blood samples for hemoglobinopathies. We wanted to find out the incidence and spectrum of hemoglobinopathies in neonates using HPLC of DBS samples and to identify the issues faced in this approach. Materials and Methods: Eluates from DBS were analyzed using Sickle Cell Short Program on Bio-Rad Variant Classic HPLC system for the presence of hemoglobins F, A, S, D, C and E. Results: Of the total 891 neonatal DBS (467 males and 424 females) examined, 876 showed a normal pattern (Hb F> Hb A). Fifteen cases (1.7 %) showed presence of hemoglobinopathies, viz. Hb S trait (6 cases); Hb D trait (5 cases); Hb E trait (4 cases). No case of homozygosity for these hemoglobinopathies was identified, as evident from the presence of HbA. The percentages of abnormal hemoglobins varied from 3.8 to 5.1 % for Hb S, 2.3-11.2 % for Hb D and 1.6-4.1 % for Hb E/A2. Conclusion: There is no policy for neonatal screening for hemoglobinopathies in India. Therefore, even though the incidence of hemoglobinopathies in neonates in this study is low, the findings justify the inclusion of testing for hemoglobinopathies in the newborn screening panels. The very small amount of blood required for this purpose and the ease of collection and transportation of the samples in the form of DBS are an added advantage.

30. **Newborn screening in India: Current perspectives**

    2010

    Indian Pediatrics

    Kapoor, S and Kabra, M

31. **Screening of asymptomatic carrier of globin disorder in marathwada region, maharashtra**

    2018

    Indian Journal of Hematology and Blood Transfusion

    Dash, P M and Kharat, K R and Bindu, R S

Aims & Objectives: Despite enhanced research focus and anti/pre-natal screening aided with genetic counselling programs for Hemoglobin (Hb) disorders such Sickle Cell Disease (SCD)/thalassemias, mortality and morbidity pattern are still worrisome. Current project supported by DST, Govt, of India aimed at direct benefit to

the patients by moleculardiagnosis, education and social awareness, i.e. a form of indirect counselling to the patients and families. Patients/Materials & Methods: Present study was carried out at Dept. of Biotechnology, Centre for Advanced LifeSciences, Aurangabad (M.S.). Marathwada region of Maharashtra is a dry, arid region including seven districts having population (187 lakh) with communities like Hindu, Muslim, Jains and Sikhs. This tertiary care Multi speciality Hospital (GMCH, Aurangabad, M.S.) based study included hospitalised subjects and their family members having alpha and beta globin disorder. Subjects included were patients and their family members, confirmed by CE-HPLC followed by haematology investigations. Detailed history of the said subjects was documented in a prescribed format with informed consent. PCR based molecular diagnosis of globin gene disorders are studied for SCD & beta thalassemia (ARMS PCR), alpha thalassemia (Multiplex PCR) and beta globin haplotype (RE-PCR). Results: Incidence of globin variants in Marathwada Region, Maharashtra. Beta Thalassemia Major-BTM, Beta Thalassemia Trait-BTT, Sickle Cell Trait-SCT, HbQ trait-QT, double heterozygote of HbQ & BTT-Q-BTT, IDA- Iron DeficiencyAnemia Discussion & Conclusion: Specific genotype-phenotype correlations ultimately will determine the course of dissemination of ourclinical and epidemiological findings. (Table Presented).

32. **Persistent splenomegaly in an adult female with homozygous sickle cell anemia**

    2006

    Hematology

    Singh, S and Singh, D K and Gupta, R and Nigam, S and Singh, T

Sickle cell anemia (SCA) is associated with repeated episodes of erythrostasis in the spleen, which lead to thrombosis and infarction of the spleen resulting in "autosplenectomy" which is usually complete by 8 years of age. We present a case of a 22-year-old female who presented with complaints of fever, bone pain and joint swelling. On examination she had pallor, icterus and moderate splenomegaly. Her hemoglobin was 7.5 g/dl. Peripheral smear showed many sickled red cells. Slide test for sickling was positive with 2% sodium metabisulphite. Hemoglobin electrophoresis revealed a single band in the hemoglobin S, D, and G region. No band was seen in the HbA & HbA2 region. HbF level was 0%. USG showed an enlarged spleen with few defined hypoechoeic lesion. We present this case because of rarity of association of homozygous SCA with splenomegaly in this age group, the confusion that echogenic lesions in spleen can create and to emphasize the risk of sequestration crises, which remains in such cases. Â© 2006 Taylor & Francis.

33. **Newborn Screening for Hemoglobinopathies and Red Cell Enzymopathies in Tripura State: A Malaria-Endemic State in Northeast India**

    2018

    Hemoglobin

    Upadhye, D and Das, R S and Ray, J and Acharjee, S and Ghosh, K and Colah, R B and Mukherjee, M B

Hemoglobinopathies are a group of inherited single gene disorders. There are reports on hemoglobin (Hb) variants identified in the tribal and non-tribal populations of Tripura State in northeastern India. This study aimed to determine the spectrum of hemoglobinopathies and enzymopathies by newborn screening in Tripura State and assess the extent of neonatal jaundice. A total of 2400 cord blood samples were collected and analyzed by high performance liquid chromatography (HPLC). Further confirmation of any abnormal HPLC was done by DNA analysis. The samples were also screened for deficiency of enzymopathies, glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate kinase. Of 2400 cord blood samples screened, 225 (9.3%) were Hb E (HBB: c.79G>A) heterozygotes, 80 (3.3%) were Hb E homozygotes and one carried Hb E-Î²-thalassemia (Î²-thal). Other Hb abnormalities were also detected including 15 Hb S (HBB: c.20A>T) heterozygotes, two Hb D-Punjab (HBB: c.364G>C) heterozygotes and two compound heterozygotes for Hb D-Punjab and Hb E. Of the 80 homozygous Hb E babies, four were non-tribal and 76 babies were tribal, and 225 patients carried Hb E trait, 141 were tribal,

while 84 were non-tribal. Of 40 G6PD deficient babies identified, 13 had coinherited Hb E and two babies had pyruvate kinase deficiency. Î± Genotyping was performed in 162 affected babies, 50 of them carried Î± gene deletions. Newborn screening programs for Hb E, other hemoglobinopathies and G6PD deficiency must be encouraged in the malaria-endemic northeastern region of India. Drug-induced hemolysis can also be avoided by screening for G6PD deficiency at birth.

34. **Three non deletional alpha gene variants identified in neonates during newborn screening for sickle cell disorders**

    2011

    Indian Journal of Hematology and Blood Transfusion

    Upadhye, D and Jain, D and Nair, S and Nadkarni, A and Ghosh, K and Colah, R

Introduction: Newborn screening for sickle cell disease gives an opportunity of early comprehensive care to reduce the morbidity by appropriate prophylactic measures. We initiated one of the first newborn screening programmes for sickle cell disease in India to understand the natural history of the disease. Three unusual alphaglobin variants were identified during newborn screening. 1,161 newborns were screened for sickle cell disease using a targeted screening approach by HPLC and confirmation by DNA analysis. Cellulose acetate electrophoresis (pH 8.9), heat stability test, alpha genotyping by mPCR and DNA sequencing helped to identify different variants. Results: Three non-deletional alpha gene variants, Hb Fontainebleau, Hb O Indonesia and Hb Koya Dora were identified in newborns. Two babies who inherited Hb Fontainebleau and Hb O Indonesia along with HbS had reduced hemoglobin (Hb) levels at birth and need to be followed up. This is the first report of Hb Fontainebleau in association with sickle hemoglobin (HbS). Newborn screening also helps to identify other variants besides HbS.

35. **An assessment of the genetic load of hemoglobinopathies by using retention time chromatogram: A Tertiary Care Hospital based study, located in Ranchi District of Jharkhand**

    2014

    Research Journal of Pharmaceutical, Biological and Chemical Sciences

    Prasad, C and Singh, S B and Mahato, T and Praksh, S and Chandra, S

Various hemoglobinopathies are one of the major public health problems in Ranchi, a district located in the northeast part of INDIA. An accurate diagnosis of hemoglobinopathies is very important for management and prevention. To estimate the occurrence of Sickle Cell Anemia and Thalassemia in suspected cases of genetic disorders by using HPLC retention time chromatogram. Blood sample of suspected cases of genetic disorders were assessed in the department of Laboratory Medicine, RIMS, Ranchi for work up of anemia or other blood related disorders. This blood samples were assessed on BIORAD variant II. Results: A total of 107 blood samples in years 2013 f were examined by HPLC retention time chromatogram. Out of these 63(58.88%) cases showed abnormal hemoglobin fractions. The major abnormality observed was of high HbA2. A cutoffvalue of >3.9% was considered for diagnosis of beta thalassemia trait (BTT). A total of 13 cases (12.1%) of BTT was diagnosed. Other hemoglobinopathies were as follows: Sickle homo 12 (11.2%), Sickle trait 10 (9.3%), dB Thal trait 9 (8.4%), Sickle Thal 7 (6.5%), Heredetery Persistent Fetal Hemoglobin (HPFH) 7 (6.5%), B Thal Major 5 (4.6%). This study revealed that genetic load of Sickle Cell Anemia and Thalassemia is 58.88% in study sample.

36. **Prenatal diagnosis of haemoglobinopathies in Odisha: A preliminary study**

    2019

    Indian Journal of Hematology and Blood Transfusion

    Panda, M and Mohanty, D and Kar, M R

Aims & Objectives: Haemoglobinopathies are the most common monogenic recessive disorders in Odisha. Prenatal diagnosis and selective termination of an affected foetus is a feasible option to decrease the disease burden. Lack of facilities for prenatal diagnosis prompted us to establish the prenatal diagnosis in first trimester of pregnancy by chorionic villi sampling (CVS) analysis. The present communication describes for the first time our experience in last 3 years consisting of 34 cases. Patients/Materials & Methods: CVS was obtained by a trained radiologist in the first trimester of pregnancy (10-12 weeks) and the dissection of the same was carried out under the dissecting microscope (Nikon SMZ800N). DNA was extracted using Spin column method (Qiagen). ARMS-PCR was used for detecting different mutations for Î²-thalassemia and Sickle Cell Anemia. GAP-PCR was done for detection of dÎ²-thalassemia. VNTR markers were used to look for maternal contamination. Results: Eight common mutations in Î²-globin gene in Indian population were detected in 33 (97%) cases by ARMS-PCR where as one case (3%) having rare dÎ² thalassemia was detected by GAP-PCR. 33 (97.05%) cases were given confirmed diagnosis using ARMS-PCR where as 1 (2.95%) case was confirmed by using ARMS & GAP PCR. Out of 34 cases, 18 (52.9%) Î² thalassemia, 9 (26.4%) SCD, 2 (5.8%) Sickle-thal, 4 (11.7%) HbE-thal and 1 (2.9%) dÎ² thalassemia. Fetal diagnosis shows 10 (29.4%) normal, 6 (17.6%) HbS trait, 10 (29.4%) Î² thal trait, 1 (2.9%) HbE trait, 1 (2.9%) dÎ² thalassemia trait and 6 (17.6%) affected foetus respectively. 19 (55.5%) couples came for prenatal diagnosis who do not have affected children, this is only because of increased awareness in the population. 88.8% of SCD cases are from western Odisha and specially Aghoria community. All the couples opted for termination of pregnancy if they have affected foetus. IVS 1-5 (Ga'C) was the commonest mutation (90%) and also two rare mutations CD41/42 (-CTTT) & CD15 (Ga'A) were encountered. Discussion & Conclusion: Utilising ARMS-PCR, GAP-PCR and VNTR, we were able to offer the foetal diagnosis in 2- 3 days time in 97% of cases.

37. Patterns of hemoglobinopathies diagnosed by high-performance liquid chromatography in and around Pune (Western Maharashtra, India): A pilot study

2016

JMS - Journal of Medical Society

Buch, A and Iqbal, B and Bordawekar, R and Jain, A and Jariwala, P and Rathod, H

Background: Hemoglobinopathies are one of the major public health problems in the state of Maharashtra, India. Their prevalence shows regional and ethnic variations. Pune, now becoming educational and IT hub cater populations from different regions. Aim: To study the pattern of hemoglobinopathies diagnosed by high-performance liquid chromatography (HPLC) in Western Maharashtra, India. Settings and Design: This pilot study was aimed to find the prevalence of hemoglobinopathies in and around Pune (Western Maharashtra, India) and identify the change in the demographic profile Materials and Methods: A total of 3465 cases received from January 2012 to December 2014 for hemoglobin variant analysis at the referral laboratory were studied for hemoglobinopathies. Samples were received from various private hospitals and laboratories in and around Pune. The samples were run on instrument manufactured by Bio-Rad Laboratories based on the principle of HPLC. Based on retention time and proportion of hemoglobin (Hb) variants different hemoglobinopathies were diagnosed and their prevalence were analyzed. Results and Conclusions: Out of total 3465 patients screened for suspected hemoglobinopathies 175 (5.05%) were found positive for abnormal Hbs with maximum number in the age group 20-30 years. We found that a maximum number of patients was of thalassemia trait with a prevalence of 3.7%, followed by double heterozygous states of Sickle cell with beta thalassemia trait, sickle cell trait, and sickle cell disease in decreasing order. Other rare variants such as Hb E disease, Hb D disease, Hb E trait, double heterozygous Hb SD, and Hb SC were also identified. We found more heterozygous states as compared to homozygous states. Prevalence was on the lower side of the normal range. Conclusion: Continuous awareness programs, mass screening of the population especially childbearing age and school going children will help in early detection of heterozygous states. This further helps in preventing severe hemoglobinopathies and reducing the morbidity and mortality.

38. Detection of pattern of hemoglobin in patients advised HPLC-a hospital based study

2012

Indian Journal of Hematology and Blood Transfusion

Raj, A and Bhattacharya, J and Dutta, U C and Gogoi, P K

Objective: Study was conducted to detect the pattern of hemoglobin and relative distribution of different variants in patients attending the Hematology department, GMCH. Methods: Present study was conducted in Department of Haematology, Gauhati medical college and hospital from 1st December 2010 to 31st July 2012. Geographical distribution of cases predominantly included parts of Assam. Patients presenting with clinical features and blood examinations indicating haemoglobinopathies were subjected to HPLC. Further tests were carried out in selected cases (sickling test, acid elution test, osmotic fragility test etc.). Result: Out of total 783 patients subjected to HPLC, 394 cases (50.38 %) were having normal Hb A. Among the 49.62% cases with abnormal hemoglobin, the most prevalent pattern was heterozygous Hb E (21.18 %) followed by homozygous Hb E (15.07 %). Compound heterozygous Hb E-b was the next commonly observed variant (6.13 %). 2.29 %had sickle cell disease; 0.26 %had sickle cell trait, 0.38 % had Hb S-b trait, while two cases (0.24 %) with double heterozygous Hb S-Hb E were observed. A single case (0.12 %) of hereditary persistence of fetal hemoglobin was noted. 0.89 % cases suffered from beta thalassemia major, while 3.06 % cases were heterozygous for beta thalassemia. Conclusion: Study shows that the prevalence of abnormal hemoglobin pattern is 49.62 %, of which the most common is noted in Hb E (36.25 %) in this part of India.

39. A systematic evaluation of a newborn screening program for sickle cell disease in Gujarat, India

2012

American Journal of Hematology

Arjunan, A and Italia, Y and Ghosh, K and Colah, R and Mehta, V and Italia, K and Krishnamurti, L

Background: Newborn screening (NBS) is an important public health measure aimed at early identification and management of affected newborns. Sickle Cell Disease (SCD), with an estimated 5,200 live births every year, is a major public health problem in India. Pre-symptomafic diagnosis, institution of pneumococcal prophylaxis and provision of comprehensive care offer the possibility of prevention of complications and improving outcome of SCD. In India, SCD is highly prevalent among autochthonous ethnic groups called scheduled tribes. These communities also have a high prevalence of extreme socio-economic disadvantage. The population of scheduled tribes in the western state of Gujarat exceeds 14 million individuals. Since 2008 NBS for SCD has been piloted in Valsad and nearby areas. NBS is currently being expanded to other tribal districts in the state. Evaluation of the NBS program is essential for guiding the implementation of NBS in Gujarat and elsewhere. Objectives: To evaluate the pre-analytical, analytical, post- analytical, and organizational aspects of a pilot NBS Program for SCD in Valsad, Gujarat, India. Methods: Using a standardized Performance Evaluation and Assessment Scheme (PEAS) for NBS (Therrell et al 2010) modified for developing countries (David-Padilla, 2010) we performed systematic evaluation of the pre-analytical, analytical, post-analytical, and organizational aspects of the pilot NBS Program for SCD in Valsad. Results: Since the inception of NBS in 2008 more than 3500 newborns have been screened using High Pressure Liquid Chromatography and Iso-electric focusing with confirmation by molecular methods. Individuals identified with SCD receive comprehensive care and families of those with sickle cell trait receive genetic counseling. Using the modified PEAS methodology the pre-analytical, analytical and post analytical aspects of the NBS program received a score of 37/46 meeting 80.4% of standards. The organizational domains received a score of 20/34 meeting 58.8% of standards. The NBS standards met and areas of improvement in organization were identified. Conclusion: These data demonstrate the feasibility of implementing NBS for SCD among communities facing extreme social disadvantage in a developing country. They provide the framework for implementation and evaluation of NBS programs for SCD in the developing world.

40. HPLC- How necessary is it for haemoglobinopathy diagnosis in India?

2003

Indian Journal of Pathology and Microbiology

Tyagi, S and Saxena, R and Choudhry, V P

Cation exchange high performance liquid chromatography (HPLC) is emerging as the method of choice for the initial screening of thalassemias and haemoglobinopathies and quantification of Haemoglobins (Hbs) like HbA, HbA2 and HbF. Since it is expensive, the present study was conducted to evaluate the need for HPLC in Indian laboratories and identify situations where it would be imperative. Eighty three patients suspected to have thalassemia and haemoglobinopathies were analysed. Both HPLC and alkaline gel electrophoresis detected 14 cases of HbE syndrome and 14 cases of HbS syndrome. However of the 14 cases diagnosed as HbD syndrome by alkaline electrophoresis, eight cases were diagnosed as Hb Q India, 1 case as HbD Iran and 5 cases of HbD Punjab on HPLC. Thirty-one cases were detected to have beta heterozygous thalassemia based on the high HbA2 levels (>3.9%) and eight cases were diagnosed as beta homozygous thalassemia by both HPLC and gel electrophoresis. One of them had an unknown Hb migrating in F-A region. Her mother also had same unknown Hb variant. In view of electrophoretic migration and retention time (RT) on HPLC, possibility of HbG - San Jose was considered. HPLC being an automated instrument is highly sensitive and specific, has high resolution and helps in quantification of various haemoglobins. However in a developing country like India where economical factors play a major role in planning for management of patients, the role of HPLC is limited.

41. Antenatal carrier screening for thalassemia and related hemoglobinopathies

2014

Indian Journal of Hematology and Blood Transfusion

Singh, K and Singh, D and Shukla, S and Sharma, S and Trivedi, S S

Objectives: In India there are around 45 million B-thalassemia carriers with carrier frequency of 1-17 % in different regions of the country, average being 3.3 %. Prevalence of sickle cell trait, HbE trait and HbD trait are 29.8, 0.9 and 0.2 %, respectively. This study is an attempt to recognise the carrier status of pregnant females in National Capital Region of Delhi and to prevent the homozygous/major births. Materials and Methods: 2,000 antenatal patients were subjected to complete blood count. All cases with microcytic hypochromic indices (MCV<77fl and MCH<27pg) were subjected to serum ferritin estimation, peripheral blood smear examination and reticulocyte count. Cases with reduced serum ferritin levels were treated as iron deficiency anemia while cases with normal or raised serum ferritin levels were screened for heamoglobinopathies by HPLC. Partners of carrier women were also identified on HPLC. The carrier couple was then referred to tertiary care centre for prenatal counselling and diagnosis. Results: 1,100/1,163 cases with microcytic hypochromic indices were of iron deficiency anemia with reduced levels of serum ferritin. The remaining 63 cases with normal serum ferritin were carriers of beta thalassemia and other hemoglobinopathies identified on HPLC. Out of 63 hemoglobinopathic carriers, 59 were of beta thalassemia trait, one case each of HbE, HbS and HbD heterozygous and one was double heterozygous for beta thalassemia and HbE. The prevalence of beta thalassemia trait was 2.95 % and other hemoglobinopthies being 0.05 % each. Two couples at risk of beta thalassemia major births were identified after screening 59/63 partners of the carriers. Conclusion: Antenatal screening for beta thalassemia and related hemoglobinopathies should be mandatory. Complete blood count and serum ferritin estimation can exclude almost all cases of iron deficiency anemia and further need not be evaluated on HPLC for identification of hemoglobinopathic carriers.

42. Preimplantation genetic testing (PGT) for beta thalassemia and other hematological disorders

2020

Indian Journal of Hematology and Blood Transfusion

Athalye, A and Naik, D and Sanap, R and Naik, N and Sanap, M and Warang, D and Dhumal, S and Padyal, P and Nair, S and Madon, P and Parikh, F

Aims & Objectives: The main objectives were to offer Preimplantation Genetic Testing (PGT) to Beta-thalassemia, sickle-cell anemia and G6PD mutations carrier couples at high risk of an affected child and use this technology for selection of HLA matched unaffected euploid embryos. Patients/Materials & Methods: For 16 couples diagnosed elsewhere with heterozygous status of hematological disorders, repeat Hbelectrophoresis and mutation analysis showed that 14 were at high risk. At our IVF centre, PGT was carried out for nine couples who were carriers of beta-thalassemia, three for sickle cell anemia, and one each for hemochromatosis and G6PD deficiency, besides other monogenic disorders. During the IVF cycle, trophectoderm cells biopsied from blastocyst stage embryos were subjected to mutation analysis followed by aneuploidy screening. Unaffected euploid embryos were selected for transfer. Prenatal diagnosis reconfirmed the PGT results. For one case with beta-thalassemia, HLA matching of embryos with the affected child was carried out followed by transfer of the single HLA matched unaffected euploid embryo. Results: Of 16 couples retested, two were normal and did not need PGT. The results of PGT for 14 couples are summarized in Table 1. For sickle cell anemia, both women delivered healthy babies. For G6PD mutation, a twin pregnancy occurred but miscarried in the first trimester. For beta-thalassemia, 6/7 (85.7%) couples delivered healthy babies. One of these was a HLA identical baby ensuring a future savior sib for the elder affected child. This is the first reported HLA matched birth from Maharashtra and the second in India. Discussion & Conclusion: Beta-thalassemia, sickle-cell anemia and G6PD deficiency are common disorders in India. Termination of multiple affected pregnancies is traumatic, hence PGT during IVF is useful to select unaffected euploid embryos for implantation. To cure an affected child by hematopoietic stem cell transplantation (HSCT), PGT can be used to select HLA matched unaffected euploid embryos to get a 'savior sibling' if a suitable donor is not available. When a couple opts for PGT, molecular re-confirmation of variants is important during pre-PGT work-up. To get unaffected, even HLA matched, chromosomally normal children, PGT through IVF is now available in India for hematological and other disorders. Awareness of this facility needs to be spread.

43. Incidence of haemoglobinopathies and usefulness of red cell indices for screening of Î² thalassemia trait

2012

International Journal of Laboratory Hematology

Munshi, N and Patil, V

Objectives: Hemoglobinopathies are a group of genetic disorders affecting approximately 4.5% of the total world population.. Among these, Î² thalassemia trait (BTT) is the commonest, it's prevalence in India being about 3.5% in the general population, higher in certain communities. Prevention of the homozygous condition can be achieved through detection of heterozygous carriers (who are usually asymptomatic), by screening the population at risk. It is important to contain cost of HB electrophoresis in a country like India where resources are limited in many cities, though the prevalence of BTT + IDA is relatively high.Hence we attempted assessing the sensitivity & specificity of various formulas based on the RBC indices already available, to find the optimum formula to screen the general population for BTT. Methods: We retrospectively analyzed blood samples received in the laboratory for HB electrophoresis over 23.5 months. A total of 376 samples were analyzed;CBC was done on all the samples on Advia 2120 & LH 500;red cell indices were used to calculate different Formulas, as shown (Table Presented) HB A2 was done by HPLC on D10 from Biorad and Ferritin on Access2 by chemiluminiscence.Subjects with an A2 > 4% were classified as BTT.Ferritin status was assessed to rule out IDA. (< 10ng/ml in males & 20ng/ml for females) Patients suspected of haemoglobinopathy but with iron deficiency were treated with iron supplements and then re-evaluated for HB A2.after correction of their iron status. Those with HB A2 > 4% despite IDA were

included in the BTT group. Results: Out of 376 samples screened the haemoglobinopathies detected were as follows: Sensitivity, Specificity, PPV & NPV of the formulas were as shown The mean & + SD of the RBC indices & HB A2 in BTT were as follows: Conclusions: The incidence of BTT in our patient population over 23.5 months was 20%, and other haemoglobinopathies was 6.9% which is relatively high.. HB S Trait, HB S + BTT & HB D all showed equal incidence. Based on the sensitivity/specificity/PPV/NPV of various formulas we concluded that no single formula was 100% specific for BTT screening. But if all are used in conjunction in the following order: Shine & Lal;Srivastava; Mentzer;England & Fraser; we can pick up BTT cases on screening,thus reducing the cost of HB electrophoresis. This would help to screen antenatal women in the rural areas.

44. Sickle cell anemia-molecular diagnosis and prenatal counseling: SGPGI experience

2012

Indian Journal of Pediatrics

Kumar, R and Panigrahi, I and Dalal, A and Agarwal, S

Objective: To study the issues and dilemmas in prenatal diagnosis of Sickle cell anemia (SCA) and to evaluate the role of genetic modifiers in counseling the families. Methods: The authors studied the genotype in 47 individuals with increased HbS and three representative families were taken as an example for describing various issues which need to be sorted out for appropriate counseling. Results: Of 47 individuals 24 were S beta thalassemia, 14were homozygous sickle cell anemia (SS) and 9 were HbS trait. In the S beta thalassemia and homozygous SS cases, anemia was presenting manifestation in all. The transfusion requirement in these varied from 0-12 transfusions/ year. Hepatosplenomegaly was seen in 27 cases (71%) and only splenomegaly in 9 cases (23.7%). Jaundice was observed in 34 cases (84.2%). All the 47 subjects (including HbS trait) were studied by Hb Variant system and underwent DNA analysis for beta globin gene mutations, alpha globin gene number and XmnI polymorphism. One or two alpha gene deletion of 3.7 kb (-Î±3.7/ Î±Î± or -Î±3.7/-Î±3.7) was found in 11 out of 47 cases whereas alpha triplication was found in 2 cases. 28 cases were heterozygous (+/-) for XmnI polymorphism, 9 were homozygous negative (-/-) and 10 were homozygous positive (+/+). Patients with SCA coinherited with Î±-thalassemia have less hemolysis as revealed by lower reticulocyte counts than with normal alpha genotype. The authors further discuss the issues and dilemmas faced during prenatal counseling of three families during this study. Conclusions: The knowledge of the relationship between genotype and phenotype, effect of the modifier genes has an important role in genetic counseling and for planning individualized treatment for sickle cell anemia. Â© Dr. K C Chaudhuri Foundation 2011.

45. Risk of miscarriage following chorionic villus sampling on 315 cases for prenatal diagnosis of Thalassemia

2014

BJOG: An International Journal of Obstetrics and Gynaecology

Dasgupta, S and Mukherjee, K and Chaudhury, K

Introduction Approximately 10 000 babies are born with Thalassemia in India every year. Prenatal diagnosis of Thalassemia is the commonest indication for Chorionic Villus Sampling (CVS) in India. The primary objective of this study was to assess the miscarriage rates following transabdominal CVS for women with Thalassemia trait carrying singleton pregnancy. Methods A retrospective longitudinal study was carried out at a diagnostic centre in Kolkata. Informed consents were obtained from all patients for transabodiminal CVS under direct ultrasonic guidance with local anaesthesia. All procedures were done by the same operator at the same clinic in 2 years between August 2011 and July 2013. The median gestation at the time of CVS was 12 weeks. All but two required single puncture. Patients were discharged immediately after the procedure on broad spectrum andibiotics for 5 days. Outcome data regarding vaginal loss, miscarriage, fetal affection, preterm labour, limb reduction and missed diagnosis were collected by direct questionnaire. Results A total of 320 CVS were performed over 2 years. Five

cases were excluded as the indications were different. Three of them were for Spinal Muscular Atrophy (SMA) and one each for Haemophilia and Sickle Cell Anaemia. 56 women were lost in follow up for various reasons. Other 259 women could be followed up, out of which 53 had already terminated pregnancy as their fetuses were shown to be affected by Thalassemia major. Out of the remaining 206 women, 185 have already delivered healthy babies and another 20 have crossed 24 weeks gestation but they are yet to deliver. There was one case of miscarriage which happened 6 days after the procedure. Conclusion CVS has the advantage of making early prenatal diagnosis of hereditary haemolytic anaemia. This allows the option of early termination of pregnancy if required. The procedure is simple, safe, low cost and can be done at the ultrasonography clinic without inpatient admission. Our results, especially the rate of miscarriage, is consistent with the data published in the world literature.

46. Sickled red blood cells in urine: A preliminary indicator for the detection of sickle cell trait

2019

Indian Journal of Pathology & Microbiology : an Official Organ of Indian Association of Pathologists & Microbiologists

Garg, Neha and Gupta, Rashmi and Kumar, Sunil and Kumar, Naresh

Editor, Sickled erythrocytes (SEry) on peripheral blood smear (PBS) followed by positive sickling or solubility test are commonly used as a screening test, while hemoglobin (Hb) electrophoresis or high-performance liquid chromatography (HPLC) confirms the diagnosis of sickle cell disease (SCD). We report an interesting case of a patient with normal hemogram and red blood cell (RBC) morphology on PBS. Noncontrast computed tomography head, serum electrolytes (sodium 137 mEq/L, potassium 4.6 mEq/L), kidney function test (blood urea 12 mg/dL, serum creatinine 0.2 mg/dL), and liver function test (serum bilirubin 0.6 mg/dL) were within normal limits.

47. Spectrum of thalassemia and hemoglobinopathies in a tertiary care diagnostic center

2016

Journal of Advanced Clinical and Research Insights

Iqbal, Mohammad Shahid and Tabassum, Aisha and Chatura, K R

Hemoglobinopathies and thalassemias are one of the most common genetic abnormalities prevalent in India and the Middle East. This study was performed to identify the distribution of abnormal types of hemoglobin (Hb) in a tertiary care diagnostic laboratory. An observational study was conducted in the Department of Hematology in a tertiary care diagnostic lab of South India to know the prevalence of hemoglobinopathies and thalassemia using high performance liquid chromatography (HPLC) as the diagnostic method. A total of 518 samples were received over a period of 6-month. All 518 samples were processed for HPLC. 407 samples were normal and 111 samples showed abnormal Hb variants. Sickle cell trait (HbS heterozygous) was diagnosed in 56 (10.8%) cases, beta thalassemia minor in 40 (7.72%) cases, and sickle cell disease (HbS homozygous) in 12 (2.5%) cases, thalassemia major in 2 (0.38%) cases and 1 (0.2%) case ofhereditary persistence of fetal hemoglobin. One of the best methods emerging for screening and detection of various hemoglobinopathies is HPLC. This study showed that CE-HPLC is a reli**a**ble tool in diagnosing the presence of abnormal Hb in suspected cases on routine hematology.

48. Molecular Screening of Hemoglobin S Variant in Anemia Patients of Eastern UP Population

2019

BioRxiv

Rai, Vandana and Yadav, Upendra and Kumar, Pradeep

Hemoglobinopathies are the most common type of inherited disease in human. in India the most frequent and clinically significant hemoglobin structural variants are HbS, HbD and HbE. The HbS mutation, in which a glutamic acid at position 6 in the Î² chain is substituted for valine Sickle cell disease is a major health problem in some parts of India. 2 ml blood sample was collected from 350 anemia patient and PCR-RFLP method was used for hemoglobin S analysis. Out of 350 samples, in four individuals, HbS mutation was found in homozygous (Î² 6/Î² 6) condition. All four individuals are Sickle cell cases. In conclusion, the percentage of Sickle cell disease was observed as 1.14% in Eastern UP anemic patients.

49. Health and Medicine - Clinical and Diagnostic Research; New Clinical and Diagnostic Research Study Findings Have Been Reported by Researchers at Department of Biochemistry (Haemoglobinopathies and b-Thalassaemia among the Tribals Working in the Tea Garden

2017

Health & Medicine Week

According to news originating from Jorhat, India, by NewsRx correspondents, research stated, "Prevalence of haemoglobinopathies and b-thalassaemia are very high in India but information about its status among the tribals working in the tea gardens of Assam is very less. According to the news editors, the research concluded: "Proper diagnostic...

50. Conventional and advanced brain MR imaging in patients with sickle cell anemia

2018

The Indian Journal of Radiology and Imaging

Issar, Pratibha and Nehra, Maya and Singh, Gurmeet and Issar, S

Background: Sickle cell disease (SCD) is an autosomal recessive hemolytic disorder; its cerebrovascular complications include silent cerebral ischemia, infarct, and brain atrophy. Conventional magnetic resonance imaging (MRI) often underestimates the extent of injury. Diffusion tensor imaging (DTI) can demonstrate and quantify microstructural brain changes in SCD cases having normal routine MRI. Objective: To identify various neurological abnormalities in asymptomatic sickle cell patients using routine MRI and to evaluate the microstructure of various regions of the brain using DTI. Materials and Methods: A prospective, randomized caseâ€“control study was conducted over a period of 2 years. A total of 58 cases of SCD and 56 age- and sex-matched controls were included. Routine MRI and DTI were performed in both the groups following a standard protocol. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were calculated in certain pre-defined regions. Primary data were analyzed using MS excel version 17. Analysis of variance test was performed and statistical significance was set at $P < 0.05$. Results: Thirty regions of interest with 60 variables were included in the final analysis. Patients with SCD showed statistically significant reduced FA values, increased ADC values, or both, clustered in several brain areas, including pons, cerebral peduncle, corpus callosum, frontal, temporal, parietal white matter, centrum semiovale, periventricular areas, basal ganglia, and left thalamus ($P < 0.05$). Conclusion: DTI is a promising method for characterizing microstructural changes, when conventional MRI is normal.

51. Mass Spectrometry-Based Diagnosis of Hemoglobinopathies: A Potential Tool for the Screening of Genetic Disorder

2016

Biochemical Genetics

Das, Rajdeep and Mitra, Gopa and Mathew, Boby and Bhat, Vijay and Ross, Cecil and Pal, Debnath and Mandal, Amit Kumar

Hemoglobinopathies are caused by point mutation in globin gene that results in structural variant of hemoglobin. While 7 % of world populations are carrier of hemoglobinopathies, the prevalence of the disease varies between

3 to 17 % across different population groups in India. In a diagnostic laboratory, alkaline gel electrophoresis and cation exchange-based HPLC (CE-HPLC) are most widely used techniques for characterization of hemoglobin variants. In the above methods, the differential surface charge of hemoglobin molecule in variants is exploited for their characterization. Sometime, co-migration of variants in gel electrophoresis and co-elution or elution with unknown retention time in automated CE-HPLC might lead to ambiguity in the analysis of hemoglobinopathies. Under such circumstances, it is necessary to use other analytical methods that provide unambiguous results. Mass spectrometry-based proteomics approach and DNA sequence analysis are examples of such alternative methods. In the present study, liquid chromatography coupled to mass spectrometry has been used for three commonly observed variants in India, e.g., HbE, HbQ India and HbD Punjab that appeared with inappropriate results in the conventional analysis. A customized hemoglobin variant database has been used in the mass spectrometry-based analysis of those three variants. Mass spectrometry-based proteomics approach was used to analyze above variant sample accurately.

52. Hemoglobin E disorder: Newborn screening program

2013

Indian Journal of Human Genetics

Wiwanitkit, Viroj

Hemoglobin E (Hb E) disorder is an important kind of hemoglobinopathy. It can be seen around the world with the highest prevalence in Southeast Asia. The screening for this disorder becomes the public health policies in many countries. The screening can be performed in several population groups. The newborn screening program for Hb E disorder is an important issue in pediatric genetics. In this brief review, the author discusses on important laboratory tests for screening for Hb E disorder in newborn

53. Imaging of sickle cell disease

1999

Pediatric Radiology

Crowley, J J and Sarnaik, S

Sickle cell disease is an important health care issue in the United States and in certain areas in Africa, the Middle East and India. Although a great deal of progress has been made in understanding the disease at the molecular and pathophysiologic level, specific treatment which is safe and accessible for most patients is still elusive. Going into the next millennium, the management of this disease is still largely dependent on early diagnosis and the treatment of complications with supportive care. Thus, diagnosis and evaluation of the complications of the disease are crucial in directing clinical care at the bedside. Modern imaging modalities have greatly improved, and their application in the patient with the sickling disorders has enhanced the decision - making process. The purpose of this article is to review the clinical aspects of common complications of the disease and to discuss imaging approaches which are useful in their evaluation.

54. Antenatal screening for identification of couples for prenatal diagnosis of severe hemoglobinopathies in Surat, South Gujarat

2013

Journal of Obstetrics and Gynecology of India

Bhukhanvala, D S and Sorathiya, S M and Sawant, P and Colah, R and Ghosh, K and Gupte, S C

Purpose: Our aim was to identify couples at risk of having a homozygous or compound heterozygous child with a severe hemoglobinopathy by antenatal screening and prenatal diagnosis in Surat, South Gujarat. Method: Pregnant women were screened for hemoglobinopathies by means of red cell indices, the solubility test, cellulose acetate electrophoresis tests, and confirmation by HPLC. Husbands of the pregnant women having

hemoglobinopathies were counseled and screened for hemoglobinopathies. The couples at risk were again counseled and referred to the National Institute of Immunohematology, where mutations in parents and fetuses were identified by molecular analysis. After prenatal diagnosis, the continuing pregnancies were followed up and infants were tested at birth. Results: Out of 3,009 women, 37.04, 52.6, and 10.3 % were in the first, second, and third trimester of pregnancy, respectively. Among those having hemoglobinopathies, 102 (3.38 %) had the Î²-thalassemia trait, 46 (1.5 %) the Sickle cell trait, and 26 (0.86) had hemoglobin variants like Hb DPunjab, Hb E, Hb DIran, Hb QIndia, Hb J Paris-I, and Hb OIndonesia. Out of the 14 couples at risk of having an affected child, 11 (78.5 %) couples opted for prenatal diagnosis. Three fetuses had homozygous Î²-thalassemia and hence the pregnancies were terminated. Follow up of normal or heterozygous fetuses confirmed the diagnosis. Conclusion: During antenatal screening, we found many Hb variants of Î² and Î± globin chains. Late antenatal registration, non-cooperation of the husband for investigation, and refusal for prenatal diagnosis are the main hurdles in the hemoglobinopathy prevention program and awareness is necessary. Â© 2012 Federation of Obstetric & Gynecological Societies of India.

55. Prenatal diagnosis of sickle syndromes in India: Dilemmas in counselling

2005

Prenatal Diagnosis

Colah, R and Surve, R and Nadkarni, A and Gorakshakar, A and Phanasgaonkar, S and Satoskar, P and Mohanty, D

Objectives: The sickle gene is prevalent in the scheduled caste and tribal populations in India. The clinical presentation of sickle cell disease is extremely variable, and there are no neonatal screening programmes. This is the first report on prenatal diagnosis of sickle syndromes in 85 couples at risk (sickle cell anemia-69; sickle thalassemia-16) from different regions in India. Most of the couples were from a low socioeconomic group and their decisions were entirely dependent on the local counselling given. We have evaluated the acceptability of prenatal diagnosis and the dilemmas faced in counselling these families. Methods: Chorion villus sampling was done in the first trimester and DNA analysis using reverse dot blot hybridization or restriction enzyme digestion with Dde1 in 65 cases. Cordocentesis was done in the second trimester and fetal blood analyses by automated HPLC in 20 cases who came late. Results: 32.9% of couples came prospectively for diagnosis. 23.5% of fetuses were affected (sickle cell anemia-18, sickle thalassemia-2). The Î²-thalassemia mutation in both cases was IVS 1-5(G- > C). All the couples with an unfavourable diagnosis opted for termination of pregnancy. Conclusion: Sickle cell anemia has a relatively benign clinical course in some tribal groups in India. This raises a dilemma whether we are justified in advising prenatal diagnosis in all such cases. Copyright Â© 2005 John Wiley & Sons, Ltd.

56. Is MRI necessary for skeletal evaluation in sickle cell disease

2015

Journal of Clinical and Diagnostic Research

Sachan, A A and Lakhkar, B N and Lakhkar, B B and Sachan, S

Background: More than 50% of the worldâ€™s cases of sickle cell anaemia are in India with an estimated population of 1.27 billion as against estimated worldâ€™s population of 7.24 billion. Aim: MRI of 103 patients of sickle cell disease were evaluated to assess the skeletal changes in proven cases of sickle cell disease and to find the incidence of bony infarcts in such patients. The conversion of red marrow to yellow marrow in these patients were also studied. Materials and Methods: Sickle cell patients with musculoskeletal pain as well as asymptomatic sickle cell patients were evaluated by MRI. The standard sequences used wereT1WI, T2WI, STIR, T1WI + Gd Contrast. Results: Persistent Red marrow was seen in axial and appendicular skeleton (62 cases). Extramedullary haematopoiesis was found in 4 cases, avascular necrosis of femur head (32 cases) and bone infarcts (46 cases) were also observed in our study. Osteomyelitis, septic arthritis and tubercular infections were

associated with sickle cell disease in our study. Conclusion: MRI is very sensitive in detecting early stages of avascular necrosis, red marrow persistence, extramedullary haematopoiesis, changes of arthritis, infections and joint effusion.

57. Sickle cell diseases: What can nuclear medicine offer?

2019

Hellenic journal of nuclear medicine

Niccoli Asabella, Artor and Altini, Corinna and Nappi, Anna G and Lavelli, Valentina and Ferrari, Cristina and Marzullo, Andrea and Loiodice, Alessandra and Rubini, Giuseppe

Sickle cell disease (SCD) is the best known haemoglobinopathy, caused by a mutation substituting valina for glutamic acid at position 6 of the beta-globin chain of adult hemoglobin A, resulting in hemoglobin S (HbS). The homozygous HbS disease (HbSS), an autosomal recessive disorder, is the most common form and the Mediterranean area, along with sub-Saharian African and India, have the highest prevalence (1%-15%). In particular, Sicily with a prevalence of 2%-5%, is among the most interested regions. However, migratory flows have led to a wider diffusion of the disease no longer confined to endemic areas. In Europe, the yearly estimate of affected births are 1,300 but more than 90% of children with SCD survive into adulthood thanks to screening programs and early available care; however, their lifespan remains shortened by two or three decades compared to general population. In Greece, the number of affected births surpassing 100,000 yearly and the total number of newborns carrying two deleterious genes, if no prevention measures are taken, is estimated to be about 120-130/year. Diagnosis of SCD is based on analysis of haemoglobin through protein electrophoresis or chromatography, that are cheap and widely available techniques, even if haemoglobin mass spectrometry and DNA analysis are techniques with high-throughput testing. Prenatal diagnosis is used in many European countries, so the number of affected newborns has significantly decreased during the last 3 years. Over the course of SCD, sickling process may cause acute and chronic abdominal pain due to vaso-occlusive crisis, bone pain often in long bones due to bone marrow infarction, chronic hemolytic anemia, splenic sequestration with rapid enlargement of the spleen, delayed sexual maturation and cholelithiasis, with important inter-indivuidual variability. Sickle hepatopathy reflects liver sickling process within hepatic sinusoids and includes gallstone disease, hepatic sequestration, hepatic sideroris, acute sickle cell hepatic crises (ASHC) and sickle cell intrahepatic cholestasis (SCIC). Clinically, it appears with fever, right upper quadrant pain, jaundice and increased serum liver function tests. These patients are repeatedly esposed to trasfused red cells that contributes to iron overload and may contribute to hepatic haemosiderosis. Increased bone turnover and resorption by osteoclasts and by marrow expansion due to activation of hematopoiesis. The hematopoietic system may expand physiologically. Computed tomography (CT) is an easily reproducible imaging method that allows the morphologic whole-body evaluation although with a high dose of radiation exposure and possible side effects from intravenous contrast media. Magnetic resonance cholangiopancreatography (MRCP) is a noninvasive technique without radiation chosen to image cholangiopathy and may be followed by the execution of endoscopic retrograde cholangiopancreatography (ERCP) in case of gallstone disease. Otherwise it can be helpful in identifying extramedullary hematopoiesis sites. Dual-energy X-rays absorptiometry (DEXA) is performed to evaluate deficit of bone mineral density (BMD), in which reduction of osteoblastic activity, high risk for necrosis may induce to fragility fractures. We recently had the experience of a typical case of a 56 years old Albanian woman with SCD, with jaundice after a long history of recurrent vaso-occlusive crisis. She was submitted to splenectomy and cholecystectomy 5 years before and since then she was treated with hydroxyurea. Hemocromatosis was excluded by genetic analysis. Hepatic biopsy (Pearl's stain) showed sinusoidal dilatation and diffuse iron accumulation in hepatocytes and Kupffer cells. Endo-hepatic jaundice was observed in MRCP images. It was interesting that DEXA examination was within normal range in both right proximal femur. This may probably be due to the presence of sclerotic lesions in the vertebrae, as was seen in the CT images. Technetium-99m-methylen bisphosphonate ((99m)Tc-MDP) skeletal scintigraphy is a higly sensitive whole-body diagnostic nuclear medicine technique able to evaluate early bone metabolic changes. Multimodality SPET/CT allows to correlate scintigraphic findings with anatomical images with higher sensitivity and specificity. The higher uptake of (99m)Tc-MDP in SCD patients is due to the activation of hematopoetic system and relies on the osteoblastic response to bone resorption as in our patient. The (99m)Tc-

MDP scan may be better than fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography ((18)F-FDG PET/CT) to show sclerotic lesions. Technetium-99m nanocolloids bone marrow scintigraphy (BMS) provides information about the assessment of the reticulum-endothelial system (RES), the whole-body distribution of functional red bone marrow and the presence and the extent of extramedullary hematopoiesis, especially in liver, spleen and bone marrow. Fluorine-18-FDG PET/CT completes the whole-body assessment with an integrated multimodal approach with high spatial resolution that evaluates the metabolic activity and the standardized uptake value (SUV) in SCD patients. Modern genetic diagnosis and gene treatment give promise for having fewer cases of SCD in the future.

58. Paper-based microchip electrophoresis for point-of-care hemoglobin testing.

2020

The Analyst

Hasan, Muhammad Noman and Fraiwan, Arwa and An, Ran and Alapan, Yunus and Ung, Ryan and Akkus, Asya and Xu, Julia Z and Rezac, Amy J and Kocmich, Nicholas J and Creary, Melissa S and Oginni, Tolulope and Olanipekun, Grace Mfon and Hassan-Hanga, Fatimah and Jibir, Binta W and Gambo, Safiya and Verma, Anil K and Bharti, Praveen K and Riolueang, Suchada and Ngimhung, Takdanai and Suksangpleng, Thidarat and Thota, Priyaleela and Werner, Greg and Shanmugam, Rajasubramaniam and Das, Aparup and Viprakasit, Vip and Piccone, Connie M and Little, Jane A and Obaro, Stephen K and Gurkan, Umut A

Nearly 7% of the world's population live with a hemoglobin variant. Hemoglobins S, C, and E are the most common and significant hemoglobin variants worldwide. Sickle cell disease, caused by hemoglobin S, is highly prevalent in sub-Saharan Africa and in tribal populations of Central India. Hemoglobin C is common in West Africa, and hemoglobin E is common in Southeast Asia. Screening for significant hemoglobin disorders is not currently feasible in many low-income countries with the high disease burden. Lack of early diagnosis leads to preventable high morbidity and mortality in children born with hemoglobin variants in low-resource settings. Here, we describe HemeChip, the first miniaturized, paper-based, microchip electrophoresis platform for identifying the most common hemoglobin variants easily and affordably at the point-of-care in low-resource settings. HemeChip test works with a drop of blood. HemeChip system guides the user step-by-step through the test procedure with animated on-screen instructions. Hemoglobin identification and quantification is automatically performed, and hemoglobin types and percentages are displayed in an easily understandable, objective way. We show the feasibility and high accuracy of HemeChip via testing 768 subjects by clinical sites in the United States, Central India, sub-Saharan Africa, and Southeast Asia. Validation studies include hemoglobin E testing in Bangkok, Thailand, and hemoglobin S testing in Chhattisgarh, India, and in Kano, Nigeria, where the sickle cell disease burden is the highest in the world. Tests were performed by local users, including healthcare workers and clinical laboratory personnel. Study design, methods, and results are presented according to the Standards for Reporting Diagnostic Accuracy (STARD). HemeChip correctly identified all subjects with hemoglobin S, C, and E variants with 100% sensitivity, and displayed an overall diagnostic accuracy of 98.4% in comparison to reference standard methods. HemeChip is a versatile, mass-producible microchip electrophoresis platform that addresses a major unmet need of decentralized hemoglobin analysis in resource-limited settings.

59. Prenatal diagnosis of sickle cell disease by the technique of PCR.

2015

Indian journal of hematology & blood transfusion : an official journal of Indian Society of Hematology and Blood Transfusion

Singh, Praneeta J and Shrivastava, A C and Shrikhande, A V

Sickle cell disease (SCD) is prevalent in Central India and causes major morbidity and mortality. There is a lack of prenatal diagnostic facility near population affected with SCD. This is the pilot study in our region with the

aim to establish prenatal diagnostic facility for the couples carrying sickle cell gene in Central India, in order to help them take an informed decision regarding fetus affected with SCD and also to calculate sensitivity of polymerase chain reaction (PCR) technique in our set up with follow up high performance liquid chromatography (HPLC) of baby's blood sample. Fetal sampling was done by chorionic villous biopsy. Extracted DNA was subjected to amplification refractory mutation system (ARMS-PCR) to detect sickle cell mutation (GAGÂ â†'Â GTG) in the sixth codon of Î² globin gene. Follow-up HPLC was done to detect baby's Hb pattern. Prenatal diagnosis of sickle cell anemia was offered in total 37 cases out of which one (2.7Â %) fetal sample was inadequate. Total 26 (70.27Â %) fetuses had AS Hb genotype, 3 (8.11Â %) had AA Hb genotype and 3 (8.11Â %) had SS Hb genotype while remaining 4 (10.81Â %) were given AA/AS Hb genotype. All couples with SS fetuses opted for MTP. Follow up HPLC was performed in 24 cases, out of which 18 (75Â %) were correlated and 6 (25Â %) were mismatched. In present study sensitivity of ARMS-PCR was 75Â %. ARMS-PCR is a simple technique to be established initially for providing rapid prenatal diagnosis to the couples with known sickle cell mutation. The sensitivity of ARMS-PCR can be increased by using suitable techniques to detect maternal cell DNA contamination.

60. Screening for the sickle cell gene in Gujarat, India: A village-based model

2013

Journal of Community Genetics

Patel, J and Patel, B and Gamit, N and Serjeant, G R

The sickle cell gene in India reaches its highest prevalence among the tribal people, many of whom are marginalized in the Indian society, living in remote rural areas which are often in the hilly regions of the Deccan plateau. Delivery of all services including health care presents special challenges which are addressed in this study by an outreach program and a mobile clinical unit. Another concern among the tribal people, a suspicion of centrally provided services conceived as being imposed from the outside, has been addressed by the concept of the Sickle Cell Swa (self) Suraksha (protection) Abhiyan (movement), which seeks to educate tribal communities in sickle cell (SS) disease so that the request for screening emanates from the community itself. This program has now screened 7,307 subjects in nine villages, finding the sickle cell trait in 23.7 % (range 18.5-30.9 %) and probable SS disease in 112 subjects. The organization of the program is described along with the delivery of results on a laminated card displaying the hemoglobin genotype, advice related to the genotype, blood group information (specifically requested by the villagers), contacts within the village sickle cell committee, and clinical contacts for medical advice. In addition, a local villager has been given basic health care training to regularly visit and monitor cases of SS disease and refer those with significant complications to the hospital coordinating the screening program. It is too early to determine the success of this program, but it represents a village-based model of detection of the sickle cell gene and care for cases with the disease which is accepted by the affected communities and may have broader implications for sickle cell disease in India. Â© 2012 Springer-Verlag.

61. Newborn screening for haemoglobinopathies by high performance liquid chromatography (HPLC): Diagnostic utility of different approaches in resource-poor settings

2014

Clinical Chemistry and Laboratory Medicine

Upadhye, D S and Jain, D L and Trivedi, Y L and Nadkarni, A H and Ghosh, K and Colah, R B

Background: Sickle cell disease is a major health burden in India. The aim of the study was to compare the diagnostic utility of two different approaches on automated high performance liquid chromatography (HPLC) for newborn screening for sickle cell disorders and other haemoglobinopathies in India. Methods: Newborn babies of sickle heterozygous mothers were tested by HPLC using two different kits, the Î²-thal short kit, which is routinely used for screening for haemoglobinopathies in most laboratories, and the sickle cell short kit which is specific only for neonatal samples. Confirmation of the sickle and Î± genotypes was done by molecular analysis. Results:

Of the 601 babies tested, 276 were normal, 284 were sickle heterozygous and 41 were sickle homozygous using the Î²-thal short kit. Using the sickle cell short kit, a discrepancy was seen in one newborn sample where a normal baby was identified as a sickle heterozygous baby. Î±-Genotyping was done in 42 babies and 16 of them had Î± gene deletions. The presence of Î± thalassaemia could be suspected in 15 of these 16 babies based on a spike at the start of the chromatogram using the Î²-thal short kit. In comparison, using the sickle cell short kit the diagnosis of Î± thalassaemia was difficult based on the percentage of the FAST peak. Further, other rare Î± chain Hb variants were also missed. Conclusions: The Î²-thal short kit was more versatile than the sickle cell short kit for screening for haemoglobinopathies in newborns in our population.

62. Neonatal screening and the clinical outcome in children with Sickle cell disease in central India

2016

PLoS ONE

Upadhye, D S and Jain, D L and Trivedi, Y L and Nadkarni, A H and Ghosh, K and Colah, R B

Background: Sickle cell disease (SCD) is a major health burden in India. The objective of the study was to establish a neonatal screening program and to understand the clinical course of children with SCD in central India. Methods and Findings: Pregnant mothers were screened for sickle hemoglobin using the solubility test. Babies were screened by high performance liquid chromatography if the mother was positive for sickle hemoglobin. The diagnosis was confirmed by molecular analysis. They received early prophylactic treatment and vaccination. Of 2134 newborns screened, 104 were sickle homozygous (SS), seven had sickle Î²-thalassemia (S-Î² thal) and 978 were sickle heterozygous (AS). The other hemoglobin abnormalities detected included HbS -Î´Î² thalassemia-1, HbSD disease-2, HbE traits-5, Î²-thalassemia traits-4, alpha chain variants-3 and HbH disease-1.These babies were followed up regularly for hematological and clinical evaluation. Pain, severe anemia requiring blood transfusions and acute febrile illness were the major complications with 59.7, 45.1 and 42.6 cases per 100 person years. Fetal hemoglobin (HbF) levels were inversely associated with vaso-oclussive crisis (VOC) and severe anemia while presence of alpha thalassemia increased the rate of painful events and sepsis. Six early deaths occurred among the SS babies. Conclusion: A systematic follow up of this first newborn SCD cohort in central India showed that 47% of babies presented within 1 year of age. In spite of the presence of the Arab-Indian haplotype many babies had severe manifestations.

63. Trimodal distribution of HbS levels in sickle heterozygotes--an useful predictor of the alpha-genotype for population screening.

1998

The Indian journal of medical research

Mukherjee, M B and Surve, R and Tamankar, A and Colah, R and Mohanty, D

The trimodal distribution of HbS levels in sickle heterozygotes has been used as an indirect approach to determine the prevalence of alpha-thalassaemia in different population groups. We used this approach to predict the alpha-genotypes of 124 sickle cell heterozygotes where the HbS concentration varied from 20 to 46 per cent with antimodes at 28.0 and 33.0. The alpha-genotypes in these individuals were also determined by Southern blot hybridization. We predicted homozygous (-alpha/-alpha) or heterozygous (-alpha/alpha alpha) alpha-thalassaemia-2 in 78 subjects by the trimodal distribution of HbS. However, actual genotyping showed that 75 patients had alpha-thalassaemia. Forty six of the 47 subjects with a normal alpha-globin genotype (alpha alpha/alpha alpha) could be predicted indirectly. The overall sensitivity was 100 per cent and specificity was 94.2 per cent with a positive predictive value of 96.2 per cent and negative predictive value of 100 per cent. As alpha-genotyping is very expensive and not feasible in most laboratories in India, we conclude that the trimodal distribution of HbS levels is a suitable method for screening for alpha-thalassaemia in population studies.

64. Newborn screening in the developing countries.

2018

Current opinion in pediatrics

Therrell, Bradford L Jr and Padilla, Carmencita D

PURPOSE OF REVIEW: We review newborn screening (NBS) publications from the developing countries to identify global progress in improving child health. RECENT FINDINGS: Many developing countries do not yet have national NBS. As infant mortality rates decline, NBS gains in public health priority. Local incidence and outcome data are used to persuade health officials to include screening in priority health spending. Congenital hypothyroidism is the most cost-effective screened condition in most countries. In sub-Saharan Africa, India and some parts of Asia, screening for hemoglobinopathies and glucose-6-dehydrogenase deficiency are also important. Expanded screening for metabolic conditions is most needed in areas of high consanguinity. Screening for hearing disorders and critical congenital heart defects is increasing globally. The largest birth cohorts are India and China, but only China has successful NBS. Reports from completed government research projects in India support initiation of NBS. SUMMARY: Government activities around NBS are increasing in India and there is increased emphasis on pilot programs for sickle cell NBS in sub-Saharan Africa. Genetic counseling training in Asia and Africa is increasing and will be helpful as part of NBS. To build successful screening programs, partnerships among health professionals, parents, policy makers and industry stakeholders are essential.

65. Newborn screening shows a high incidence of sickle cell anemia in central India

2012

Hemoglobin

Jain, D L and Sarathi, V and Upadhye, D and Gulhane, R and Nadkarni, A H and Ghosh, K and Colah, R B

There is limited data on the incidence of sickle cell anemia in Central India; we therefore conducted a study to estimate the incidence of this disease in Central India. Mothers who delivered a live baby at the Government Medical College, Nagpur, India were screened for the presence of the sickle cell hemoglobin {Hb S: [Î²6 (A3) Glu â†'Val, GAG >GTG]} using the solubility test within 48 hours of delivery. Infants of mothers who showed the presence of Hb S then underwent Hb analysis by high performance liquid chromatography (HPLC). A total of 8243 mothers was screened, 1178 of whom were positive. One thousand, one hundred and sixty-two infants of mothers with a positive solubility test underwent Hb analysis by HPLC; 530 infants were normal, while 536 were heterozygous for Hb S (sickle cell trait), 88 babies were homozygous for Hb S (sickle cell anemia), while another eight babies had other Hb abnormalities. The incidence of sickle cell anemia was highest in the Scheduled caste group (1:50). We concluded that the incidence of sickle cell anemia is high in central India. Â© 2012 Informa Healthcare USA, Inc.

66. Assessment of renal function in Indian patients with sickle cell disease

2017

Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia

Lakkakula, B.V.K.S. and Verma, H K and Choubey, M and Patra, S and Khodiar, P K and Patra, P K

Sickle cell disease (SCD) and its variants are genetic disorders resulting from the presence of a mutated form of hemoglobin. Renal disease is one of the most frequent complications, and kidney damage starts very early and progresses throughout life causing severe complications. The present study is aimed to analyze creatinine-based estimated glomerular filtration rate (eGFR) in 616 SCD patients (507 HbSS and 109 HbSB+), receiving medical

care at outpatient wing of Sickle Cell Institute, Chhattisgarh. Glomerular filtration rate (GFR) estimated using the Modification of Diet in Renal Disease (MDRD), Cockcroft-Gault, chronic kidney disease epidemiology collaboration (CKD-EPI) (<17 years analyzed with Schwartz), and SCD specific Jamaica Sickle Cell Cohort Study (JSCCS)-GFR equations were compared. Further, eGFR calculated using the CKD-EPI and Schwartz equations was used to define various stages of kidney function and compared with clinical and hematological variables. The mean age of patients was 15.8 years. Comparison of eGFR using various formulas revealed that MDRD and JSCCS formulas overestimated the GFR. Among SCD patients, prevalence of glomerular hyperfiltration (GHF) is high followed by renal insufficiency (RI) and renal failure (RF). However, no differences were found in hematological profiling among different functional stages of kidney. Age and body surface area are significantly more in SCD individuals with normal kidney function and GHF. Participants with RF showed a higher level of blood urea and fetal hemoglobin. In summary, this is the first study to analyze different functional stages of kidney among SCD patients of India. Our study revealed that the GHF and RI are the important indicators of kidney damage.

67. Antenatal screening for haemoglobinopathies: current status, barriers and ethics

2019

British Journal of Haematology

Chakravorty, S and Dick, M C

Sickle cell disease (SCD) and thalassaemia are genetic disorders that are caused by errors in the genes for haemoglobin and are some of the most common significant genetic disorders in the world, resulting in significant morbidity and mortality. Great disparities exist in the outcome of these conditions between resource- rich and resource-poor nations. Antenatal screening for these disorders aims to provide couples with information about their reproductive risk and enable them to make informed reproductive choices; ultimately reducing the likelihood of children being born with these conditions. This review provides an overview of the current status of antenatal, pre-marital and population screening of SCD and thalassaemia in countries with both high-and low prevalence of these conditions, methods of screening in use, and discusses some of the pitfalls, ethical issues and controversies surrounding antenatal screening. It also discusses outcomes of some screening programmes and recognises the need for the establishment of antenatal screening in areas where their prevalence is highest; namely sub-Saharan Africa and India.

68. The Chhattisgarh state screening programme for the sickle cell gene: a cost-effective approach to a public health problem

2015

Journal of Community Genetics

Patra, P K and Khodiar, P K and Hambleton, I R and Serjeant, G R

In India, the Chhattisgarh State screening programme for sickle haemoglobin focuses on children aged 3â€“15Â years and has screened over 1,050,440 subjects over the last 6Â years. Commencing in the District around the capital Raipur, this programme has now completed screening in 7 of the 27 Districts of Chhattisgarh State. Screening is initially performed by solubility tests on fingerprick samples in the field and those with positive tests have venipunctures for haemoglobin electrophoresis. The frequency of the sickle cell trait was 9.64Â % and of the SS phenotype 0.29Â % with only two Districts in Hardy-Weinberg equilibrium, most Districts showing an excess of the SS â€˜phenotypeâ€™ most readily explained by symptomatic selection. The estimated costs were US$0.28 (solubility tests alone) and US$0.60 (haemoglobin electrophoresis). Of the social groupings commonly used in India, the OBCâ€™s (other backward classes) had the highest frequencies of the sickle cell gene mutations, followed by the Scheduled Tribes and the Scheduled Castes. The objectives of the programme were the detection of sickle cell disease for prospective clinical management and of the sickle cell trait for purposes of genetic counselling. The former objective is being met for diagnosis although the success of referral to clinic services requires audit. The objective of genetic counselling is compromised by the failure of the screening test to

detect other genes of potential clinical significance such as HbD Punjab and the beta thalassaemia trait. Despite these exceptions, the detection of HbS appears relatively robust and could be another condition factored into the traditions of partner selection amongst the underprivileged communities of this state. Overall, the Chhattisgarh programme seeks to address the daunting challenges of large populations carrying the sickle cell gene and maybe a useful model for elsewhere.

69. Guidelines for screening, diagnosis and management of Hemoglobinopathies

2014

Indian Journal of Human Genetics

Ghosh, K and Colah, R and Manglani, M and Choudhry, V P and Verma, I and Madan, N and Saxena, R and Jain, D and Marwaha, N and Das, R and Mohanty, D and Choudhary, R and Agarwal, S and Ghosh, M and Ross, C

The Î²-thalassemias and sickle cell disorders are a major health burden in India. Diagnosis and management of these disorders both in adults and in newborns using appropriate approaches and uniform technology are important in different regions of a vast and diverse country as India. In view of a National Thalassemia Control Program to be launched soon, a need was felt for guidelines on whom to screen, cost-effective technologies that are to be used as well as for establishing prenatal diagnosis programs in regional centers. Newborn screening for sickle cell disorders is in its infancy in India and uniform approaches need to be followed. Also, included are guidelines for monitoring and managing patients who are now growing older and need comprehensive care as well as management of complications of the disease.

70. Profiling Î²-thalassaemia mutations in India at state and regional levels: implications for genetic education, screening and counselling programmes.

2009

The HUGO journal

Sinha, S and Black, M L and Agarwal, S and Colah, R and Das, R and Ryan, K and Bellgard, M and Bittles, A H

Thalassaemia and sickle cell disease have been recognized by the World Health Organization as important inherited disorders principally impacting on the populations of low income countries. To create a national and regional profile of Î²-thalassaemia mutations in the population of India, a meta-analysis was conducted on 17 selected studies comprising 8,505 alleles and offering near-national coverage for the disease. At the national level 52 mutations accounted for 97.5% of all Î²-thalassaemia alleles, with IVSI-5(G>C) the most common disease allele (54.7%). Population stratification was apparent in the mutation profiles at regional level with, for example, the prevalence of IVSI-5(G>C) varying from 44.8% in the North to 71.4% in the East. A number of major mutations, such as Poly A(T>C), were apparently restricted to a particular region of the country, although these findings may in part reflect the variant test protocols adopted by different centres. Given the size and genetic complexity of the Indian population, and with specific mutations for Î²-thalassaemia known to be strongly associated with individual communities, comprehensive disease registries need to be compiled at state, district and community levels to ensure the efficacy of genetic education, screening and counselling programmes. At the same, time appropriately designed community-based studies are required as a health priority to correct earlier sampling inequities which resulted in the under-representation of many communities, in particular rural and socioeconomically under-privileged groups. ELECTRONIC SUPPLEMENTARY MATERIAL: The online version of this article (doi:10.1007/s11568-010-9132-3) contains supplementary material, which is available to authorized users.

71. Screening for the sickle cell gene in Chhattisgarh state, India: An approach to a major public health problem

2011

Journal of Community Genetics

Patra, P K and Chauhan, V S and Khodiar, P K and Dalla, A R and Serjeant, G R

The aim of this study is to determine the feasibility of large-scale population screening for the sickle cell gene in high risk areas with limited resources. A programme designed to detect the sickle cell trait and sickle cell disease has screened 359,823 subjects among 2,087 (99.7%) of the villages in Raipur District, Chhattisgarh State, India between October 2007 and June 2010. Children aged 3-15 years were initially screened in the villages by solubility tests on fingerprick samples. Venipuncture was performed on subjects with positive solubility tests, and the samples were transferred to Raipur Medical College for alkaline haemoglobin electrophoresis. The sickle cell trait occurred in 33,467 (9.30%) and an SS phenotype in 747 (0.21%). The gene frequencies were not in Hardy-Weinberg equilibrium most likely due to a deficiency of the SS phenotype failing to enter the sampled population from either sickness or early death. Subjects with abnormal haemoglobin genotypes may factor this information into decisions regarding marriage and avoid the risks of having children with sickle cell disease. The techniques described may be a model for other developing societies with limited resources. Â© Springer-Verlag 2011.

72. Newborn Screening for Sickle Cell Disease: Indian Experience.

2018

International journal of neonatal screening

Colah, Roshan B and Mehta, Pallavi and Mukherjee, Malay B

Sickle cell disease (SCD) is a major public health problem in India with the highest prevalence amongst the tribal and some non-tribal ethnic groups. The clinical manifestations are extremely variable ranging from a severe to mild or asymptomatic condition. Early diagnosis and providing care is critical in SCD because of the possibility of lethal complications in early infancy in pre-symptomatic children. Since 2010, neonatal screening programs for SCD have been initiated in a few states of India. A total of 18,003 babies have been screened by automated HPLC using either cord blood samples or heel prick dried blood spots and 2944 and 300 babies were diagnosed as sickle cell carriers and SCD respectively. A follow up of the SCD babies showed considerable variation in the clinical presentation in different population groups, the disease being more severe among non-tribal babies. Around 30% of babies developed serious complications within the first 2 to 2.6 years of life. These pilot studies have demonstrated the feasibility of undertaking newborn screening programs for SCD even in rural areas. A longer follow up of these babies is required and it is important to establish a national newborn screening program for SCD in all of the states where the frequency of the sickle cell gene is very high followed by the development of comprehensive care centers along with counselling and treatment facilities. This comprehensive data will ultimately help us to understand the natural history of SCD in India and also help the Government to formulate strategies for the management and prevention of sickle cell disease in India.

73. Multicenter Evaluation of HemoTypeSC as a Point-of-Care Sickle Cell Disease Rapid Diagnostic Test for Newborns and Adults Across India.

2020

American Journal of Clinical Pathology

Mukherjee, Malay B and Colah, Roshan B and Mehta, Pallavi R and Shinde, Nikhil and Jain, Dipty and Desai, Shrey and Dave, Kapilkumar and Italia, Yazdi and Raicha, Bhavesh and Serrao, Erik

Objectives: Sickle cell anemia is the commonest genetic disorder in India, and the frequency of the sickle cell gene is very high in the remote tribal areas where facilities are generally limited. Therefore, a rapid and affordable point-of-care test for sickle cell disease is needed.Methods: The diagnostic accuracy of HemoTypeSC was

evaluated against automated high-performance liquid chromatography (HPLC) as the gold standard for its efficacy in a newborn screening program.Results: A total of 1,559 individuals (980 newborns and 579 adults) from four participating centers were analyzed by both methods. HemoTypeSC correctly identified 209 of 211 total hemoglobin (Hb) SS cases, for a 99.1%/99.9% total HbSS sensitivity/specificity. Overall, HemoTypeSC exhibited sensitivity and specificity of 98.1% and 99.1% for all possible phenotypes (HbAA, HbAS, and HbSS) detected. HPLC is relatively expensive and not available in most laboratories in remote tribal areas.Conclusions: We conclude that the rapid, point-of-care testing device HemoTypeSC test is suitable for population and newborn screening for the HbS phenotype.

74. Neonatal screening of sickle cell anemia: a preliminary report.

2012

Indian Journal of Pediatrics

Panigrahi, S and PK, Patra and PK, Khodiar and Panigrahi, Sumanta and Patra, Predeep Kumar and Khodiar, Prafulla Kumar

Objective: To evaluate feasibility of systematic neonatal screening for sickle cell disease in Chhattisgarh.Methods: A pilot study was done from February 2008 through January 2009 in Department of Pediatrics & Neonatology, Pt. J.N.M. Medical College & Dr.B.R.A.M. Hospital, Raipur (Chhattisgarh) on a total of 1,158 neonates. Blood samples from the neonates were taken after 48 h of birth on filter paper for detection of sickle cell anemia using Biorad hemoglobin variant Neonatal sickle cell short programme by high performance liquid chromatography (HPLC). On follow up, cases were analyzed by HPLC using Beta thalassemia short program to rule out false negative case and other hemoglobin variants.Results: Of the 1,158 neonates screened, 628 were boys (54.2%) and 530 were girls (45.8%). Sickle cell disease was found in 3 cases (0.2%) (95%C.I 0.12-0.28), sickle cell trait was found in 68 cases (5.8%) (95%C.I 4.5-7.5). After 6-9 mo of age three cases of sickle cell diseases were reinvestigated, out of which one case turned out to be double heterozygous for sickle cell and beta thalassemia trait. Fourteen preterm neonates reported as normal in initial screening were called for follow up after 6 mo of age, 10 infants reported in OPD and 4 lost in follow up. These 10 infants were reinvestigated; 2 had sickle cell disease, 1 had sickle cell trait and 7 infants were normal. Sixty eight cases of sickle cell trait found with initial screening were also called for follow up after 6 mo of age; 61 cases reported in OPD between 6 mo to 1 y of age and 7 cases lost in follow up. Sixty one infants were reinvestigated; 60 had sickle cell trait and 1 had sickle cell disease which was reported earlier as Sickle cell trait (FAS). Thus on total follow up of cases, there were 5(0.4%) sickle cell disease, 61(5.26%) sickle cell trait, 1(0.08%) double heterozygous for sickle cell and beta thalassemia trait which needs mutation studies for thalassemia characterization (s/Î²(0) or s/Î²(+)).Conclusions: Early detection of sickle cell disease (SS) done by neonatal screening will help in early prevention and management of complications in postnatal period.

75. Assessing the impact of screening and counselling high school children for Î²-thalassaemia in India

2007

Journal of Medical Screening

Colah, R and Thomas, M and Mayekar, P

76. Continuing diagnostic relevance of the sickling test in the era of CE-HPLC

2013

Indian Journal of Hematology and Blood Transfusion

Kumar, M and Sharma, P and Kumar, V and Bhargava, M

77. **Prenatal diagnosis of sickle cell anemia using polymerase chain reaction.**

1993

Indian pediatrics

Bankar, M P and Kate, S L and Ranade, S A and Barnabas, R J and Mokashi, G D and Phadke, M A and Hegde, M V

78. **Feasibility of a Newborn Screening and Follow-up Programme for Sickle Cell Disease among South Gujarat (India) Tribal Populations.**

2015

Journal of Medical Screening

Italia, Yazdi and Krishnamurti, Lakshmanan and Mehta, Vishal and Raicha, Bhavesh and Italia, Khushnooma and Mehta, Pallavi and Ghosh, Kanjaksha and Colah, Roshan

79. **Newborn screening for sickle cell disease in India: the need for defining optimal clinical care.**
2014

Indian Journal of Pediatrics

Patel, Jyotish and Serjeant, Graham R

80. **Rapid mid-trimester prenatal diagnosis of beta-thalassaemia and other haemoglobinopathies using a non-radioactive anion exchange HPLC technique - an Indian experience**

1997

Prenatal Diagnosis

Rao, V B and Natrajan, P G and Lulla, C P and Bandodkar, S B

Anion exchange high performance liquid chromatography (AX-HPLC) has been widely used for separating and quantifying various haemoglobin fractions especially in the haemoglobinopathies. We have evaluated the reliability of this technique to measure low concentrations of adult haemoglobin (HbA) in fetal blood to enable differentiation between affected and unaffected fetuses at risk for Î²-thalassaemia (85) and other haemoglobinopathies such as Î´Î²/Î²-thalassaemia (1), E-Î²-thalassaemia (2), S-Î²-thalassaemia (1), and sickle cell anaemia (1). The HbA Values obtained ranged between 0 and 9.51 per cent. The HbA for 27 affected fetuses was 0 per cent, while two showed a HbA value of 0.5 per cent. The mean HbA for 61 unaffected fetuses was 4.8 Â± 2.08 per cent. Thirty cord blood samples (cord abortus in cases of affected fetuses and cord full term in cases of unaffected fetuses) were analysed to reconfirm the diagnosis. Ten babies between 8 and 18 months of age could be followed up for confirmation. AX-HPLC was found to be a simple and rapid procedure with high sensitivity and there was a good correlation between the HbA values obtained by AX-HPLC and the diagnosis by carboxymethyl cellulose (CMC) chromatography.

TREATMENT

1. **Posterior Reversible Encephalopathy Syndrome in HSCT for Hemoglobinopathies**

   2019

   Biology of Blood and Marrow Transplantation

   Doval, D and Choudhary, D and Sharma, S and Khandelwal, V and Kumar, M and Setia, R and Handoo, A

Introduction: HSCT is the only curative treatment for thalassemia major (TM) & sickle cell disease (SCD) with excellent outcomes. However it is associated with several complications. Cyclosporine (C) and Tacrolimus (T) are frequently used for prevention of GvHD and neurotoxicity is one of the complications of these drugs. PRES is a serious complication seen more often with TAC than CSA. PRES is a clinico-radiological entity that is characterized by varied neurologic symptoms including seizures; bilateral gray & white matter edema. Herein we report our experience of PRES in HSCT in Hemoglobinopathies. Material & Methods: This is a retrospective analysis of patients with TM & SCD who underwent transplant at our institute between February 2010 - September 2018. A total of 250 transplants were done for patients with Hemoglobinopathies during this period (TM = 213 & SCD = 37)(Table 1) Results: Out of 250 HSCT, 21 patients (8.4%) developed PRES during transplant course; 16 patients (7.5%) were with TM & 5 patients (13.5%) were of SCD (table 2). At the median follow up of 516 days; the OS and DFS for TM was 81.25% and 75% respectively. For SCD; the OS & DFS at the median follow up 299 days was 100% & 60% respectively. TRM was 18.75% in TM cohort and none in SCD patients. Conclusion: PRES should be considered in patients presenting with hypertension or seizure post HSCT. SCD patient have higher incidence of PRES possibly due to associated sickle cerebral vasculopathy. The overall outcome is good without any long term neurological sequlae.

2. **Preoperative Automated Red Cell Exchange in Sickle Cell Disease: Experience at Apollo Hospitals, Chennai**

   2010

   Vox Sanguinis

   Menon, R

Background: Red Cell Exchange is used to manage the Vaso-occlusive complications of Sickle Cell Disease (SCD). In our hospital we used the automated Red Cell Exchange in 10 patients with SCD as a preoperative procedure in 2009. Aim: Use of the Automated Red Cell Exchange in the preparation of patients with SCD for major surgery and thereby contribute to better patient care and management. Methods: Ten patients with SCD were referred to our center for preoperative Automated Red Cell Exchange. Eight patients were scheduled for hip replacement surgery, one for mitral valve repair and one for a splenectomy. All of them underwent 2-3 sittings of Red Cell Exchange by the Hemonetics Plus Aphaeresis machine. The manufacturer's instructions were followed under the guidance of a transfusion medicine consultant. Transfusion support was provided using antibody screened, compatible blood. Results: There was a significant and satisfactory reduction in the percentage of HbS in all the patients. The procedure was well tolerated. Postoperative period was uneventful and satisfactory. Conclusions: It is concluded that appropriate use of automated Red Cell Exchange in the preoperative preparation of patients with SCD helps in improved surgical outcome and contributes to better patient care.

3. **Hematopoietic stem cell transplant for sickle cell disease: Single center experience from North India**

2016

Bone Marrow Transplantation

Kharya, G and Doval, D and Choudary, D and Khandelwal, V and Kaul, E and Lunkad, S and Pessi, K and Handoo, A and Dadu, T and Dhamija, G and Setia, R and Sharma, B and Sharma, S

Introduction: Sickle cell anemia (SCA) remains associated with high risks of morbidity and early death. Even best of supportive care fails to improve quality of life. Hematopoietic stem cell transplant can be considered for selected group of patients. In the long run it is not just economical but also substantially improves quality of life. We report our experience with HSCT in a group of children affected by SCA. Material (or patients) and methods: Nine consecutive patients suffering from SCA who underwent HSCT between March 2014 and November 2015 were included in the study. Three underwent matched sibling donor bone marrow transplant (BMT), one patient underwent mismatched unrelated donor peripheral blood stem cell transplant (PBSC) and one underwent matched sibling cord blood transplant (CBT) using Busulfan@3.2 mg/kg/ day x 4 days, cyclophosphamid@50 mg/kg/day x 4 days, hATG (PfizerATGAM)@30 mg/kg/day x 3 days. One adult patient underwent matched sibling donor PBSC using reduced intensity conditioning with busulfan@3.2 mg/kg/day x 4 days, cyclophosphamid@60 mg/kg/day x 2 days, ATG(PfizerATGAM) @30 mg/kg/day x 3 days. Immune suppression for BM/PBSC patients was cyclosporine@3 mg/kg/day in 2 divided doses starting D-3 and methotrexate@10/m2 on D+1 followed by 7 mg/m2 on day 3, 6 and 11 post BMT and cyclosporine and methylprednisolone for CBT. Three patients underwent haploidentical HSCT using hypertransfusion (target Hb 11-13gm/dl) and hydroxyurea (20 mg/kg) from day -45, conditioned with Thiotepa 10mg/kg in two divided doses (D-7), fludarabine 30 mg/m2 (D-6 to D-2), cyclophosphamide 14.5 mg/kg (D-5, D-4), TBI 2 Gy with thymic shielding (D-1), rATG (Genzyme Thymoglobulin 1.5 mg/kg (D-9 to D-7). GVHD prophylaxis included PTCy 50 mg/kg/day on D3 and 4, tacrolimus to maintain a level of 5-15 ng/ml (till 6 months post HSCT) & MMF (till D35) starting from D5. Results: The median age of patient's was 4.5 years (range 1-29 years). Before transplantation all patients had repeated episodes of veno-occlusive crisis and acute chest syndrome. One had stroke and hip replacement secondary to avascular necrosis of hip joint. Of the 9 patients, 8 survived without sickle cell disease, with Lansky/Karnofsky scores of 100. At median follow up of 235 days (range 19-607) the probabilities of survival, SCA-free survival, and transplant-related mortality after transplant were 89%, 89%, and 11%, respectively. One child who underwent haploidentical HSCT died of grade IV acute gut GVH on day 53 post HSCT. All surviving patients remained free of any SCA-related events after transplantation. Conclusion: Outcome of HSCT in SCA has improved significantly. With better conditioning regimens, improved supportive care, the outcome of alternative donor transplant (matched unrelated donor, mismatched unrelated donor, haploidentical) and adult SCA has improved and matches matched sibling donor transplant. HSCT should be strongly considered as a curative modality for selected patients suffering from SCA.

4. **Trials of hydroxyurea in sickle cell hemoglobinopathies patients of eastern India**

2012

Indian Journal of Hematology and Blood Transfusion

Purohit, P and Kumar Patel, D and Patel, S and Dehury, S and Bishwal, S C and Meher, S and Pradhan, B and Das, K

Introduction: Increased level of HbF (22.3 Â± 6.9) was found to have protective effect against painful crisis, osteo-necrosis, ACS and splenic dysfunction in Sickle cell disease patients of Odisha (Mashon RS, 2009). Low dose Hydroxyurea (10 mg/kg body-wt/day) effectively increased the level of HbF in this patients (Patel DK, 2012). Unfortunately, the use of HU is extremely limited in India, because of its high cost and the apprehension of its toxicities. Objective: To assess the clinical and haematological response of low dose Hydroxyurea in patients of sickle cell hemoglobinopathies in eastern India. Materials and Method: The study was undertaken at Sickle

Cell Clinic & Molecular Biology Laboratory, V.S.S. Medical College, Burla, Odisha, India, from 2006 to 2012. 1887 patients were enrolled including 1738 HbSS (35.7 % paediatrics and 64.3 % adults), 125 HbS-b thalassemia (33.6 % paediatrics and 66.4 % adults), 18 HbSD and 6 HbSE. The indication were>3 VOC or>2 blood transfusion in last 12 months of presentation. Detailed baseline studies, i.e. CBC, HPLC, Bio-chemical, liver function test were done and cases were followed up at three month intervals. Here we analysed the data of 364 cases under regular follow-up for more than 2 years of HU therapy. Result: After 2 years HU therapy %HbF increased significantly from 18.6 Â± 6.9 to 22.5 Â± 7.3 but the proportionate rise of HbF varied from case to case. MCV, MCH and MCHC level also increased significantly in all cases. The frequency of painful crises reduced significantly after HU therapy. In paediatric cases response rate was 71.5 % where as in adults it was 91.2 %. Following HU therapy, about 95.0 % patients became transfusion independent. Transient bone marrow suppression (Absolute Neutrophil Count <2,500/lL, platelet count<80,000/lL) was occurs in 6.96 % cases. Discussion: With a minimal dose (10 mg/kg body-wt/day) of HU, most of the patients showed an impressive improvement in clinical and haematological parameters. In resource poor country like India, low dose HU therapy provides a suitable therapeutic option for a vast number of untreated sickle cell hemoglobinopathies patients.

5. **Experience with low dose thalidomide in transfusion dependent beta thalassaemia in a resource limited setting**

   2019

   Blood

   Mehta, P and Yadav, N and Soni, P and Thekuddan, S F and Singh, R and Khushoo, V and Mirgh, S P and Agrawal, N and Ahmed, R and Kapoor, J and Bhurani, D

Introduction Thalassemia is the most prevalent inherited hemoglobinopathy characterized by defective synthesis of Î² chain, leading to ineffective erythropoiesis. In India, 3.2% (1 in every 25 people) are carriers of beta thalassemia. Management of thalassemia includes transfusion support, adequate iron chelation and prevention of undue extramedullary erythropoiesis. Red blood cell aggregation, aggregate strength and oxygen transport potential of blood are abnormal in both homozygous sickle cell anemia and sickle-hemoglobin C disease. Both clinicians and families of these patients realize that the main challenge is obligation of life long blood transfusion and iron chelation therapy in order to have a normal life. Thalidomide, an immunomodulatory drug, has therapeutic effect in fetal Hemoglobin (HbF) induction but exact mechanism of action is not known yet. Hence, this drug has been tried in thalassemia intermedia (TI) and had shown significant effect in decreasing transfusion requirement. Primary aim of our study was to evaluate the clinical response of thalidomide and/or Hydroxyurea (HU) in transfusion dependent beta thalassemia (TM and TI). The secondary aim is to study the toxicity profile of this drug in our study population. Methods It is a retrospective study which included beta TM and TI patients from August-2015 to November-2018, who received thalidomide with or without hydroxyurea. Dose used was 10-20 mg/kg/day & 25-100 mg/day for HU and thalidomide respectively. Study was approved by Institutional Review Board. Results We studied 167 patients (TM=129 and TI=38) with males (n= 111) and median age 14 (0.5-31) years. At presentation, median size of liver and spleen was 4 (1-12) cms and 3 (1-16) cms respectively. Nineteen patients were post splenectomy. Median age at first transfusion was 9 (1-144) months. Median duration between transfusions was 20 (10-180) days. Median packed cell transfusion per year was 18.2 (2-36.5). (Table-1). Median dose of HU was 500 (250-500) mg & thalidomide was 50 (25-100) mg. Median duration of thalidomide therapy was 9 (1-73) months and HU was 8 (1-183) months. Median Hb post treatment at day 90 for TI was 9.1 gm/dl (6.7-13) gm/dl and TM was 9.1 (6.2-13) gm/dl. Median duration of transfusion free period was 15 months (1-38 months) till last follow-up. Post treatment median size of liver and spleen was 3 (2-11) cms & 2 (1-14) cms respectively. Increased duration between transfusions was observed in 17 patients with median duration of 40 (18-90) days between transfusions. Most common toxicities observed were constipation=1, neutropenia=9, deranged liver function =6 followed by skin rash=4. Thrombosis, Hepatitis-A and excessive fatigue was seen in 1 patient each. At last follow-up, 78 (46.7%) patients were transfusion free whereas 37 (22.1%) were transfusion dependent, duration of transfusion increased in 17 (10.2%) patients, 3 (1.2%) patients abandoned treatment and 6 (3.6%) patients to be assessed yet as they didn't complete their 3 months of therapy at last follow-up. No follow-up records available for 26 (15.5%) patients so response could not be assessed. Conclusion With the use of minimal doses of

thalidomide, transfusion independency and thereby reduction in iron overload can be achieved in patients with transfusion dependent beta thalassemia patients. But one needs to be cautious to monitor the side effects commonly encountered in our study. Large population studies and longer follow ups are required to define the potential use of this immunomodulatory drug in hemoglobinopathies, which can be an effective and affordable treatment option for transplant ineligible patients. (Table Presented).

6. **Global treatment satisfaction levels and treatment patterns from the international sickle cell world assessment survey (SWAY):hydroxyurea (HU) versus no HU**

   2020

   Blood

   El Rassi, F A and James, J and Andemariam, B and Inusa, B P D and Francis-Gibson, B and Nero, A C and Minniti, C P and Trimnell, C and Abboud, M R and Arlet, J.-B. and Colombatti, R and de Montalembert, M and Jain, S and Jastaniah, W and Nur, E and Pita, M and Ramscar, N and Bailey, T and Rajkovic-Hooley, O and Osunkwo, I

Background: SWAY was a cross-sectional survey that assessed the global impact and treatment ofsickle cell disease (SCD) (James et al. ASH 2019). SCD puts patients at risk of multiple complicationsdriven by vaso-occlusion and hemolytic anemia. Vaso-occlusive crises (VOCs) are the hallmark ofSCD and can require healthcare attention. VOC frequency may be reduced by HU (Charache et al. NEngl J Med 1995). Aims: We assessed self-reported symptoms and quality of life (QoL) indicators for patients whoreported using HU at the time of SWAY versus patients who did not, and we collected data on alltreatments reported by SCD patients, by geographical region. Data were also collected regardinghistorical patient-reported use of HU prior to SWAY but these are not included here. Methods: SWAY was completed between April and October 2019 by SCD patients from 16 countriesacross 6 regions. A limitation is that Asia and South America were represented by single countries(India and Brazil, respectively). SWAY was completed by proxy (parent/guardian/caregiver) forpatients aged 6-11 years and could be optionally self-completed by patients aged â‰¥12 years. Opinionswere captured using a 1-7 Likert scale for some questions (5-7 indicated highsatisfaction/impact/agreement). SWAY did not assess treatment outcomes. Results: Of 2145 patients, 652 (30%) reported receiving HU at the time of SWAY (56% female; 50%aged 6-25 years); 1493 patients reported not receiving HU at the time of SWAY (51% female; 59%aged 6-25 years). The number of patients reporting HU use varied regionally (Table). Patients whoreported using HU also reported a lower VOC burden than patients who did not report using HU atthe time of SWAY (median: 3 vs 4 VOCs in the 12 months before SWAY, respectively). However,considering other symptoms commonly experienced in the month prior to SWAY, a greaterproportion of patients who reported using HU experienced these symptoms than patients who didnot report using HU, except for headache and poor appetite, which were experienced by a lowerproportion of patients who reported HU use (Figure). Similar proportions of patients reported thatSCD had a high impact (Likert scale 5-7) on emotional wellbeing (61% [reported HU use at time ofSWAY] vs 59% [did not report HU use at time of SWAY]) and daily activities (39% vs 40%,respectively). Overall, when including dietary supplements, the most common treatment reported at the time ofSWAY in all regions except the Middle East was folic acid. Common treatments varied regionallywhen excluding supplements (Table). Top treatment goals for patients in all regions were to improveQoL and prevent SCD worsening. Treatment satisfaction (range: 57-92%) was highest in Asia (Table).Over 70% of patients wanted alternatives to their ongoing pain medications in all regions, exceptAsia (44%).

7. **The role of hydroxyurea and valproic acid in the management of severe HBE-Î² thalassaemia**

   2014

   Indian Journal of Hematology and Blood Transfusion

   Biswas, S and Chaudhuri, S and Kumar, M and Sen, A and Bhattyacharyya, M and Ghosh, K

Summary: We evaluated the efficacy of HbF inducing agents (hydroxyurea and valproic acid) in E-beta thalassemia. We found Hydroxyurea is effective in significant increases in HbF levels. Introduction: Hb E-beta

thalassemia is a common disorder in eastern India with varying clinical presentation. Pharmacological induction of fetal haemoglobin is shown to reduce disease severity in sickle cell disease. We evaluate the efficacy of hydroxyurea and valproic acid in Hb E-beta thalassemia. Materials and Methods: Patients with severe Hb E-beta thalassemia were randomised to receive either hydroxyurea (10 mg/kg) or valproic acid (5 mg/kg). Patients were followed up for response with frequent scheduled visits. Results: Baseline parameters for patients in both arms were matched as shown in Table 1. All patients were followed prospectively for transfusion requirement, drug effectiveness and toxicity. With median follow-up of 6 months, we found hydroxyurea to be associated with significant increases in HbF levels (Table 2). Conclusions: Hydroxyurea as compared to valproic acid results in significant increase in HbF and decrease in serum ferritin, although it does not translate into reduced transfusion requirement. Longer follow- up with more number of patients is warranted for confirmation of these findings. (Table Presented).

8. **The effect of hydroxyurea on the expression of white blood cell adhesion molecules in patients with sickle cell disease**

   2014

   Research Journal of Pharmaceutical, Biological and Chemical Sciences

   Ghafourian, M and Keikhaei, B and Mohseni, A R and Chinipardaz, R

Sickle cell disease is an autosomal recessive disorder that appears as a serious chronic hemolytic anemia. Vaso-occlusive crisis is the most important cause of morbidity and mortality in these patients. Recent findings showed that the expression of leukocyte adhesion molecules on vascular endothelium increased the risk of vaso-occlusive crisis in these patients. This study was conducted to identify adhesion molecules mainly involved in vaso-occlusive crisis and the effect of hydroxyurea on the expression of leukocyte adhesion molecules in patients with sickle cell disease. In this analytical study, patients were divided into two groups. In this regard, 21 patients who suffered sickle cell disease and received hydroxyurea, and 21 patients who suffered sickle cell disease but did not receive hydroxyurea. The control group comprised 21 healthy people. A blood samples was drawn from all participants, and a CBC test was performed to determine WBC count and percentage of neutrophils, lymphocytes, monocytes, and eosinophils. After Lysis of red blood cells by lysine, blood samples were stained with four types of monoclonal antibodies against surface antigens of CD11a, CD11b, CD18, and CD62L and analyzed using flow cytometry. Finally, the expressions of these markers on leukocytes were recorded as percent values. The indexes used for the three groups were compared to one another using SPSS software, ANOVA, and Tukey test. WBC count in patients was significantly higher than that in the control group. However, after using hydroxyurea, it decreased significantly in patients (P- valueâ‰¤ 0.05). Percentage of neutrophils was high in patients, but it decreased significantly after using hydroxyurea. The analysis by flow cytometry showed that the expression of CD11a, CD11b, CD18, and CD62L markers on leukocytes increased in patients compared to that in the control group. The expression of these markers in patients with sickle cell disease significantly decreased after using hydroxyurea (P-valueâ‰¤ 0.05). The expression of leukocyte adhesion molecules increased in patients with sickle cell disease compared to that in normal participants. As leukocytosis and increased expression of adhesion molecules in patients with sickle cell disease decreased significantly after using hydroxyurea, vso-occlusive crisis can be prevented by the use of hydroxyurea as an important strategy in pharmacological approaches.

9. **Phytochemical characterization of twelve medicinal plants used for sickle cell disease management in chhattisgarh**

   2015

   International Journal of Pharma and Bio Sciences

   Gupta, A and Sharma, S and Verma, H K and Tyagi, D S and Mishra, P K and Patra, P K

Medicinal plants can be a source of succour in the control of sickle cell disease (SCD) in Chhattisgarh. The lower strata of the state rely heavily on traditional medicine due to their cultural alignment as well as their

inability to afford the cost of treatment offered by orthodox medical practitioners. Twelve plant species have been selected to examine their phytochemical constituents from SCD prone areas of state currently used to the management of disease. Qualitative analysis of phytochemical constituents' viz. tannins, flavonoids, terpenoids, saponins, phenol, steroids, phlobatannins, carbohydrates, glycosides, coumarins, alkaloids, proteins, emodins, anthraquinones, anthocyanins, leucoanthocyanins and quantitative analysis of alkaloids, tannin, saponins, flavonoids and total phenol was performed by the standard protocol available in the literature. Quantitative analysis of alkaloid, tannin, saponin, flavonoids and total phenol had revealed that Momordica charantia possessed maximum alkaloid (5.92%w/w) and tannin (9.44%w/w), Aloe vera highest saponin (7.15%w/w) & flavonoids (8.23%w/w) and Allium sativum highest total phenol (12.43%w/w) content. Present findings will be very compassionate to elaborate our study objectives to investigate better management options and reduce the symptomatic crisis of SCD.

10. **Use of transcranial and extracranial sonography to predict stroke in sickle cell disease children**

    2018

    European Journal of Neurology

    Gupta, V M and Garg, R and Gupta, S

Background: To establish which vessel evaluation in Transcranial Doppler (TCD) and Extracranial doppler (ECD) is ideal in sickle cell disease among all the ves-sels.Evaluation of Extracranial carotid vessels has not been done in previous published studies. Material and Methods: This was a prospective study carried out in the Department of radiodiagnosis. Unispital Healthcare, India from April 2016 to August 2017. Selection of cases: 50 normal individuals as control group and 50 cases of pathologically confirmed sickle cell disease fortranscranial and CarotidDoppler-study assessthe Doppler values. Inclusion criteria: Newborn to15 yrs with no deficits on neurological examination and approval & informed consent of subject's caretaker. Exclusion criteria: Patient with history of hydroxyurea therapy in sickle cell patient,major head injury requiring visit to an emergency deptatr-ment, seizure disorder requiring anticonvulsant therapy and history of prenatal and perinatal hypoxic ischae-mic brain injury. Methodology: All the selected patients were evaluated with detailed clinical history, clinical examination. The children were placed in supine position for extracranial doppler and sitting position for transcranial doppler. Results: In our study, out of 50 sickle cell children, 5 children with higher velocities were given transfusion. The difference of mean velocity before transfusion and after transfusion was approx. 20-25 cm/sec on both sides.This shows that transfusion reduces the risk of stroke by reducing the velocities whichwas well corre-lated with the literature. Conclusions: Our study can act as benchmark in extracranial Doppler studies of sickle cell patients. We have not followed the patients of sickle cell disease till stroke, but we can say with certainty that increased values of velocity >200 cm/s is an absolute indication for blood transfusion to prevent stroke, which was observed in 10% of sickle cell patient in our study where velocities reduced by 20-25 cm/sec after blood transfusion.

11. **Anesthetic management of patients with sickle cell disease posted for bipolar prosthesis**

    2020

    Indian Journal of Forensic Medicine and Toxicology

    Agrawal, S and Deshmukh, P and Deshmukh, P and Modak, A

In case of surgical procedures in sickle cell disease (SCD), patients are associated with high risk of perioperative complications like vaso-occlusive crisis, chest syndrome, post-operative infections, congestive heart failure, cerebrovascular accident and acute kidney injury. Preoperative assessment and stabilization like control of sepsis, blood transfusion, correction of hypoxia, hypothermia, dehydration and acidosis is needed to reduce peri-operative complications. Blood transfusion (Simple, manual exchange and automated exchange) remains an important therapeutic intervention in patients with SCD. The case study below shows the perioperative management of

patients posted for bipolar prosthesis due to AVN (avascular necrosis). Adequate analgesia, incentive spirometry, early mobilisation and oxygen supplementation is the mainstay of post-operative management.

12. **Atrial septal defect closure on cardiopulmonary bypass in a sickle cell anemia: role of hydroxyurea and partial exchange transfusion.**

    2010

    Annals of cardiac anaesthesia

    Gosavi, K S and Dash, S K and Shah, B N and Upasani, C B

Partial exchange transfusion during cardiopulmonary bypass, while conducting cardiac surgery may be a useful technique in patients with high level of sickle hemoglobin. Along with this preoperative use of hydroxyurea and alternative analgesic modalities such as transcutaneous electrical nerve stimulation in postoperative period may be beneficial, in our opinion. A 16-year-old female of Turner's syndrome having sickle cell anemia scheduled for closure of arterial septal defect on cardiopulmonary bypass was managed with partial exchange transfusion and warm cardioplegia.

13. **Non-transfuion dependent thalassemia: A therapeutic challenge**

    2014

    Indian Journal of Hematology and Blood Transfusion

    Singh, A K and Mohanty, P and Das, B P

Summary: A 7 year old female child presented with progressive pallor with splenomegally (10 cm) was diagnosed as sickle-Beta thalassemia. She gave h/o recurrent vaso occlusive crisis requiring BT-1-2 units at an interval of 6-8 months. Introduction: Non transfusion dependent thalasemia is a distinct entity characterized by no regular blood transfusion for survival. A variety of clinical complications,mild tomoderate elevation of serumferritin and paradoxically a high iron overload in the tissue or organ. Materials and Methods: Hb-8gm/dl, Reti count-2.4 %, LDH-380 IU/L, S.ferritin-945.7 ng/ml and Transferrtin saturation-58 %, liver biopsy shows iorn overload detected in Prussian blue stain which was disproportionately high in compariosion to Serum ferritin level. Echocardiography appeared normal with EF-74 %. The child was treated with hydroxyurea 20 mg/kg, Deferasirox-10 mg/kgwithFolvite andSodamine.Onfollow up after 1 year S.ferritin was -735 ng/ml and liver biopsy showed depleted iron deposition. Result: The child was experienced improvement physically along with improvement in the haematological parameters. Conclusion: In absence of increased hemolysis and regular BT increased iron deposition in the tissue can be attributed to increased iron absorption in the G.I. bed due to decreased hepcidin. Sickle-beta cell thalassemia coulde be considered as NTDT syndrome. Monitoring and management of iron overload should be adopted occasionally.

14. **The effect of antioxidant supplementation on the oxidant and antioxidant status in sickle cell Anaemia**

    2012

    Journal of Clinical and Diagnostic Research

    Hundekar, P S and Suryakar, A N and Karnik, A C and Valvi, R and Ghone, R A and Bhagat, S S

Background: Sickle cell anaemia is a hereditary disorder, associated with severe haemolytic anaemia, periodical vasoocclusive pain and premature death. Oxidative stress is one of the factors that may enhance the rate of haemolysis by damaging the erythrocyte membrane by lipid peroxidation. Aim: The present study was carried out to investigate the oxidant and antioxidant status in sickle cell individuals and the effect of antioxidant supplementation on oxidative stress. Material and Method: A total of 90 subjects participated in the study, including 30 heterozygous (HbAS) and 30 homozygous (HbSS) sickle cell patients and 30 age and sex matched

healthy controls. Oxidative stress was evaluated by measuring the levels of serum malondialdehyde (MDA), plasma protein carbonyl, serum nitric oxide (NO), the erythrocytic activity of superoxide dismutase (SOD) and catalase and the total antioxidant capacity (TAC) of plasma before and one month after of antioxidant supplementation. Results: The baseline levels of MDA, protein carbonyl, NO and the activity of SOD were significantly ($p<0.001$) elevated in the HbSS and HbAS groups as compared to those of the controls. The baseline level of the activity of catalase and the TAC of plasma were significantly ($p<0.001$) decreased in the HbSS and HbAS groups as compared to those in the controls. After the supplementation of the antioxidants, we found a significant ($p<0.001$) decrease in the levels of MDA, protein carbonyl, NO and in the activity of SOD, while there was a significant ($p<0.001$) increase in the level of activity of catalase and in the TAC of plasma in both the groups of sickle cell patients. Conclusion: The values of both the oxidants and the antioxidants did not meet that of the controls, thus suggesting a spontaneous generation of free radicals that consumed the antioxidants. Therefore, antioxidant supplementation is essential in sickle cell individuals in the steady state as well as in illness, to prevent the oxidative damage to the erythrocytes.

15. **Haploidentical hematopoietic stem cell transplant for sickle cell disease using thiotepa based reduced intensity conditioning and post transplant cyclophosphamide**

    2015

    Bone Marrow Transplantation

    Kharya, D G and Doval, D and Chaudhary, D R and Dhamija, M and Khandelwal, V and Lunkad, S and Setia, R and Handoo, A and Sharma, S and Dadu, T

Introduction: Hematopoietic stem cell transplant (HSCT) can cure sickle cell disease (SCD). This option is however limited by availability of matched sibling or related unaffected donors. Over the years results of haploidentical transplants have improved significantly. Bolanos et al reported successful haploidentical HSCT for SCD using post transplant cyclophosphamide (PTCy) however there cohort had almost 40% risk of rejection. We report a child with SCD with complications being successfully treated using thiotepa based reduced intensity conditioning along with PTCy. Materials (or patients) and methods: 3 year old boy with SCD on regular transfusions was taken up for haploidentical HSCT from father in the absence of suitably matched donor. He was started on hypertransfusion (target Hb 11-13gm/dl) and hydroxyurea (20 mg/kg) from day -45. He was conditioned using Thiotepa 10 mg/kg in two divided doses (D-7), Fludarabine 30 mg/m2 (D-6 to D-2), Cyclophosphamide 14.5 mg/kg (D-5, D-4), TBI 2 Gy with thymic shielding (D-1), Thymoglobulin 1.5 mg/kg (D-9 to D-7). GVHD prophylaxis included PTCy 50 mg/kg/day on D3 and 4, Tacrolimus to maintain a level of 5-15 ng/ml (till 6 months post HSCT) & MMF (till D35) starting from D5. Patient received unmanipulated GCSF primed bone marrow harvested from his father with a target MNC > 8x108/kg. He received 9.03x10âˆ§8/kg mononuclear cells, 8.41x10âˆ§6/kg CD34 cells. Results: Polymorphonuclear cell and platelet engraftment were seen on D+12 and D+15 respectively. Whole blood chimerism on day +15 showed 99.45% donor cells. There is no evidence of acute or chronic GVHD. He was discharged on D+20 in good clinical condition. He is currently D+80 post HSCT clinically well, on tacrolimus. Post HSCT his sickle percentage has gone down from 88% to 22%, chimerism D+60 post HSCT is 99.62%. Conclusion: Successful Haploidentical Paternal HSCT for SCD using thiotepa based conditioning and PTCy. This appears to be a promising technique in haploidentical or MMUD HSCT with early and sustained engraftment and less risk of GVHD. This is the first reported case of haploidentical HSCT using this technique of sickle cell disease in India.

16. **Hematopoietic stem cell transplant for sickle cell disease: The Indian experience**

    2017

    Bone Marrow Transplantation

    Kharya, G and Raj, R and Yadav, S P and Mathews, V and Katewa, S and Choudhary, D and Sharma, S and Khandelwal, V and George, B and Srivastava, A and Easow, J

Introduction: Sickle cell disease (SCD) remains associated with high risks of morbidity and early death. Even best of supportive care fails to improve quality of life. Hematopoietic stem cell transplant (HSCT) can be considered for selected group of patients. In long run it is not just economical but also substantially improves quality of life (QOL). We report our experience with HSCT for SCD from India Material and methods: Seventy three consecutive patients suffering from SCD who underwent HSCT between Jan 2006 and November 2016 were included in the study. Fifty two underwent matched sibling donor (MSD), 2 matched family donor (MFD), 3 matched unrelated (91/0 or 10/10), 2 cord blood transplant CBT (1 matched sibling cord blood and 1 matched unrelated) and 15 patient underwent haploidentical transplant. Different conditioning regimens were used and so was the graft versus host disease prophylaxis depending on institutional protocols as depicted in table 1. (Table presented) Results: A total of 73 patients underwent SCT. The median age was 9 years (10 months-29 years). M/F ratio was 45/28. Majority of patients were either from African union or Oman. All patients suffered from one or other severe symptoms making them eligible for SCT. Graft source was bone marrow (BM) in 30 with median CD34 count of 5.3x106/kg (0.92-10.7), peripheral blood (PB) in 36 with median CD34 count of 8.5x106/kg (3.9-20.18), cord blood in 2 with median CD34 count of 1.27x105/kg (0.44-2.1) and combined BM & PB in 5 with median CD34 count of 6.37x106/kg (1.5-23.3). Of the 73 patients, 61 are alive and disease free with Lansky/Karnofsky scores of 100. There were 8 deaths (4 MSD/MFD/MUD 3 haploidentical and 1 matched unrelated CBT). Four patients rejected the graft (2 haploidentical and 2 MSD/MFD/MUD). At the last follow up, the probabilities of survival, SCD-free survival, and transplant-related mortality were 89%, 83.5%, and 11%, respectively. Conclusion: Outcome of HSCT in SCD has improved significantly. With better conditioning regimens, improved supportive care, the outcome of alternative donor transplant and adult SCD has improved and matches sibling donor transplant. HSCT should be strongly considered as a curative modality for selected patients suffering from SCD.

17. **Vitamin D and anesthesia: Is our present knowledge sufficient?**

    2014

    Journal of Anaesthesiology Clinical Pharmacology

    Goudra, B and Singh, P

18. **Managing thalassaemia- Indian experience**

    2011

    Vox Sanguinis

    Singh, V

Overview: Thalassaemia is one of the major hereditary disorders involving haemogloblin in the human blood, which accounts for high mortality in childhood the name of a group of genetic blood disorders. Is a major clinical problem and unless supported by transfusion, children suffer from growth retardation and die at an early age from the profound effects of anemia. Thalassaemia and the haemoglobinopathies are a major health problem, placing an immeasurable emotional, psychological and economic burden on millions of people around the world. In the West, substantial progress has been made towards understanding the pathology of thalassaemia and its treatment. But the fact remains that the treatment of thalassaemia is a costly and painful process. In developing countries, knowledge of the disease remains sparse and treatment is an unaffordable luxury. Epidemiology: Globally, over 500,000 children with Hb disorders born annually 70% in middle and low resource countries. Out of which about 70% sickle cell anaemia and 30% thalassaemia syndromes. Less than 500,000 patients with Hb disorders are registered (living). Thalassemia in India the prevalence shows the estimated number of thalassemics in India is 1,00,000. On an average 8-10 thousand thalassaemia majors born in India every year. Recommended treatment: Regular blood transfusion on a life long basis until a cure is available Transfusion regimes should aim to keep patients Hb levels at between 9- 10.5 g/d1 before transfusion and not more than 15 g/d1 after transfusion. Ideal Blood Transfusions: A unit of 250 ml packed red cells to be transfused every 3- 4 weeks and blood transfusion to

take place in Thalassemia Centre under proper medical care with regular Chelation. Treatment: Many children die undiagnosed and even after diagnosis, death often occurs due to anemia, infection, cardiac failure. Not more than 10-15% of thalassaemia majors receive adequate treatment. The Cost of maintaining good treatment $2090.00-$4180.00 per year. Challenges: Threat is growing as it is estimated that about 60,000-70,000 are born each year world over with B-thalassaemia major. Out of which 8000-10,000 are born each year in India (approx 20%). By 2020 the figure will reach 2,12,000 from 1,00,000. Cure of Thalassemia: 1. Stem Cell Transplantation. 2. Cord Blood Transplantation. 3. Gene Therapy. 4. Hydroxyurea- Some drugs, including Hydroxyurea, can stimulate production of a third type of protein chain called gamma chains. In the womb, the fetus makes this type of protein instead of beta globin. Way forward: It is Safe Blood transfusion, adaptation of National plan, access to free treatment and value of prevention is recognized. In spite of high prevalence the counseling and health education regarding inherited disorder before marriage is required and needs to avoid the marriage between two traits. In is important that genetic counseling of the new born before birth for thalassaemia traits.

19. Pediatric haploidentical stem cell transplantation with post-transplantation cyclophosphamide for non-malignant disorders: A feasible option

2016

Bone Marrow Transplantation

Yadav, S P and Thakkar, D and Rastogi, N and Kohli, S and Nivargi, S and Chopra, Y R and Katewa, S

Introduction: Due to unavailability of matched related donor many children needing transplant are unable to avail this treatment as unrelated donor are either not available or too expensive for most children in the developing countries like India. T-cell replete haploidentical stem cell transplantation (SCT) with post-transplantation cyclophosphamide (PTCy) has shown encouraging results for the treatment of hematologic malignancies. However this technique has rarely been applied to treat non-malignant disorders. Here we present our experience using same in 19 children with various nonmalignant disorders. Material (or patients) and methods: Donors were mobilized with Granulocyte colony stimulating factor 10 microgram/kg daily for four days, the PBSC were collected with one large volume apheresis procedure. The conditioning was with Fludarabine, Cyclophosphamide, Thioptepa and total body irradiation in all 16 children, Fludarabine and Treosulfan in 2 (age less than 1) and Fludarabine and Busulfan in 1.Serotherapy was part of conditioning, Rabbit Anti-thymoglobulin 4.5 mg/kg in 16 and Campath 1 mg/kg in 3. All received post transplant cyclophosphamide (PT-Cy) 50 mg/kg on day 3 and 4 as graft vs. host disease (GVHD) prophylaxis along with tacrolimus and mycophenolate mofetil. After a signed informed consent, 19 patients who needed a transplant, were allografted; median age was 3 years (range 1-18), 18 were boys and 1 girl, the diagnosis were: Primary immunodeficiency-6, thalassemia major-7, sickle cell disease-3, pure red aplasia-2, acquired aplastic anemia-1. Results: All the donors shared 5 out of 10 alleles with the recipient; in 42% of the cases the donor was the Mother, in 32% the Father and in other 26% one sibling. A median of 10 million of CD34cells/kg was infused (range 5-24 million/kg). Three children died before engraftment (2 due to multi-drug resistant bacterial sepsis and one due to stroke).The engraftment rate was 84%, median time to achieve 500 neutrophil or more was 15 days (range 13-21) and a self- sustained platelet count of 20.000 or more was 12 days (range 9-20). Chimerism at day+100 was available in 16 cases; 14 of them had full donor hematopoiesis. One had mixed chimerism and 1 fully recipient and both had thalassemia. One with mixed chimerism had rejection despite giving one dose of donor lymphocyte infusion (2 x 104/kg). Both of them underwent second PBSCT from a different haploidentical donor (one TCR alpha-beta depleted and other T cell replete) and both engrafted but one died of Veno-occlusive-disease (VOD) and other with BK virus encephalitis. The median follow-up of remaining patients is 13 months (range 3-30), the cumulative incidence of graft versus host disease (GVHD) acute and chronic extensive was 26% and 16% respectively. Grade-III acute GVHD was seen in 2 patients. Three patients have died, the causes were; Post-transplant lympho-proliferative disoder-1,Veno-occlusive disease-1 and Myxedema -1. Overall 58% children are alive and diseases free at last follow up. Conclusion: The use of T-cell replete haploidentical SCT with PTCy and a reduced intensity conditioning for treating pediatric non-maligant disorder is feasible and a good alternative for children with non-malignant disorders and without suitable matched donors.

20. **Obstructive uropathy: Is it always urolithiasis?**

    2015

    Indian Journal of Nephrology

    Jain, V and Sureka, B and Bansal, K and Arora, A

{Figure 1}{Figure 2} Renal papillary necrosis (RPN) is a clinical condition that arises due to impairment of blood circulation to papillary tip of renal medulla due to diabetes mellitus, sickle cell disease, pyelonephritis, renal vein thrombosis, analgesic abuse, genitourinary tuberculosis and obstructive uropathy.

21. **Effective control of sickle cell disease with hydroxyurea therapy**

    2010

    Indian Journal of Pharmacology

    Singh, Harminder and Dulhani, Navin and Kumar, Bithika and Singh, Prabhakar and Tiwari, Pawan

Objective : Hemoglobin F augmentation is another approach to treat sickle cell disease (SCD). This study evaluates the efficacy and impact of Hydroxyurea (HU) on fetal hemoglobin (HbF) and other hematological parameters, which result in decreasing the painful crisis and lower hospital admissions. Materials and Methods : A prospective study was carried out in the Department of Medicine, Government Medical College, Jagdalpur. Twenty-seven patients with SCD received HU at a mean dose of 22 mg/kg/d. The baseline results were analyzed and compared with the post treatment result, at the end of one year. Statistics : Student's t-test was used to determine the level of significance. Results : Twenty-four patients completed a one-year period successfully; a significant increase was noted in the mean HbF%, from 12.83 to 19.17, and the mean corpuscular volume (MCV) from 82.57 to 89.87 Fl. The mean hospital admission (numbers) in the last one year decreased from 4.75 to 2.25 and the mean number of SCD crisis for the last one year decreased significantly from 3.63 to1.67. Conclusion : We found a significant reduction in hospital admissions, a reduction in the overall sickle cell crisis and an associated improvement in HbF% without any significant side effects in the patients with SCD, treated with HU.

22. **Fetal Globin Stimulant Therapies in the Beta-hemoglobinopathies: Principles and Current Potential**

    2008

    Pediatric Annals

    Perrine MD, Susan P

It has long been established that fetal globin chains interfere with pathological polymerization of sickle hemoglobin, and that high levels of HbF correlate with mild or benign clinical courses in sickle cell disease.1-7 Hemoglobin F (HbF) levels >20% in sickle cell anemia with hereditary persistence of fetal hemoglobin (S-HPFH) syndromes and in certain populations, such as the Eastern Saudi Arabian-Indian populations, ameliorate the symptoms of sickle cell disease, and result in generally benign courses.1-3 High levels of HbF and F/F-cell confer survival advantage, protect against most complications of sickling disorders, and thus have become targeted goals of therapies to induce HbF in sickle cell disease, from the average levels of 5% to 8% in patients after the hemoglobin switch is complete.1-17 The beta-thalassemia syndromes are heterogeneous, caused by >200 molecular mutations affecting the beta globin gene complex, with decreased synthetic ratios of non-alpha to alphaglobin chains, precipitation of excess, unbalanced alpha-globin chains, and accelerated programmed cell death of erythroblasts at the polychromatophilic stage.8-17 Affected patients become anemic after the fetal (gamma) globin genes are suppressed postnatally.

23. Intravitreal bevacizumab (Avastin) for the treatment of proliferative sickle retinopathy

2008

Indian Journal of Ophthalmology

Shaikh, Saad

[1] Although we are unable to state whether anti-VEGF therapy changes the long-term history and prognosis of the disease and incidence of future complications, intravitreal bevacizumab injection may have a role in the primary and/or adjunct therapy of neovascular complications of sickle cell retinopathy.

24. Gene Therapy - A Cure for All

2013

Medical Buyer

Carrier status of an individual for diseases including thalassemia, Tay-Sachs disease, sickle cell disease, cystic fibrosis, phenylketonuria, spinal muscular atrophy, homocystinuria, hematochromatosis, phenylketonuria, glycogen storage disease, congenital adrenal hyperplasia, Bloom's syndrome, Canavan disease, Factor XI deficiency, dysautonomia, mediterranean fever, Fanconi anemia, G6PD deficiency, Gaucher disease, and glycogen storage disease can be determined.

25. Hematopoietic stem cell transplantation for hemoglobinopathies: Progress and prospects

2008

Indian Journal of Medical and Paediatric Oncology

Krishnamurti, Lakshmanan and Gupta, D

Allogeneic bone marrow transplantation from an HLA-identical donor is currently the only means of curing thalassemia. Transplant outcome depends upon the presence of risk factors (hepatomegaly, portal fibrosis and poor quality of chelation). patients are defined to have class I - if no risk factor, class II with one or two and class III - if all three risk factors are present. For patients under 16 years of age, for class I, class II and III the probabilities of survival are approximately 95%, >80% and 60-70%, respectively. The risk of transplant related morbidity& mortality is low when transplant is done at an early age. Currently, busulfan, cyclophospahmide and antithymocyte globulin based combination is used for conditioning. More than 200 patients with sickle cell disease (SCD) have undergone allogeneic SCT with long term survival in >80% of patients. Results are better if donor is an HLA-identical sibling and if transplant is done early in the course of disease. Presently, experience with reduced intensity SCT and matched unrelated donor transplant is limited to recommend their routine use.

26. Anaesthetic challenges in a child with sickle-cell disease and congenital heart block

2016

Indian Journal of Anesthesia

Bala, Indu and Sahni, Neeru and Mitharwal, Sanwar

Post-operative analgesia was maintained with paracetamol 500 mg IV 8 th hourly and fentanyl boluses of 30 ÃŽÂ¼g as rescue analgesic whenever visual analogue scale exceeded 3. [5] To conclude, perioperative anaesthetic management of children suffering from SCD and CHB needs meticulous pre-operative and intra-operative management and post-operative vigilance for preventing sickle-cell crisis and associated complications.

27. Search for antisickling agents from plants

2013

Pharmacognosy Reviews

Dash, Bisnu and Archana, Y and Satapathy, Nibarana and Naik, Soumendra

The sickle cell disease is fatal in nature. Thousands of children are dying off due to this health problem throughout the globe. Due to the rapid development of diagnosis and clinical managements such patients are living up to a respectable age. But as there is no permanent cure the patients are suffering from bone and joint pain, jaundice, hepato-splenomegaly, chronic infections etc. The main physiological complicacy is due to the polymerization of sickle hemoglobin (HbS), (sickling process) inside the red blood cell (RBC) of these patients during deoxygenating state. The change of RBC from spherical to sickle shape is due to the polymerization of mutant hemoglobin (HbS) inside the RBC and membrane distortion during anoxic condition. The mechanism and the process of sickling are very complex and multifactor in nature. To get rid from such complicacies it is necessary to suitably and accurately stop the sickling of RBC of the patients. The potential anti-sickling agents either from natural sources and/or synthetic molecules may be helpful for reducing the clinical morbidity of the patients. A lot of natural compounds from plant extracts have been tried by several workers in recent past. Most of the studies are based on in vitro red cell sickling studies and their mode of action has not been properly understood. Although, few studies have been in vivo in nature pertaining to transgenic sickle animal model, there is paucity of data on the human studies. The result of such studies although has shown some degree of success, a promising anti-sickling agent is yet to be established.

28. Mechanical versus electrical detachment of coils in treatment of intracranial aneurysms: Role in sickle cell disease

2018

Neurologia i Neurochirurgia Polska

Dutta, Gautam and Sachdeva, Deepashu and Singh, Daljit and Singh, Hukum and Kumar Srivastava, Arvind

29. Cardiac surgery in patients with sickle cell disease

2013

Journal of Postgraduate Medicine

Khandeparkar, J and Porwal, M and Mahajan, V

30. Optimizing hydroxyurea therapy for sickle cell anemia

2015

Ware, R E

Hydroxyurea has proven efficacy in numerous clinical trials as a disease-modifying treatment for patients with sickle cell anemia (SCA) but is currently under-used in clinical practice. To improve the effectiveness of hydroxyurea therapy, efforts should be directed toward broadening the clinical treatment indications, optimizing the daily dosage, and emphasizing the benefits of early and extended treatment. Here, various issues related to hydroxyurea treatment are discussed, focusing on both published evidence and clinical experience. Specific guidance is provided regarding important but potentially unfamiliar aspects of hydroxyurea treatment for SCA,

such as escalating to maximum tolerated dose, treating in the setting of cerebrovascular disease, switching from chronic transfusions to hydroxyurea, and using serial phlebotomy to alleviate iron overload. Future research directions to optimize hydroxyurea therapy are also discussed, including personalized dosing based on pharmacokinetic modeling, prediction of fetal hemoglobin responses based on pharmacogenomics, and the risks and benefits of hydroxyurea for non-SCA genotypes and during pregnancy/lactation. Another critical initiative is the introduction of hydroxyurea safely and effectively into global regions that have a high disease burden of SCA but limited resources, such as sub-Saharan Africa, the Caribbean, and India. Final considerations emphasize the long-term goal of optimizing hydroxyurea therapy, which is to help treatment become accepted as standard of care for all patients with SCA.

31. **The Potential of mHealth as a Game Changer for the Management of Sickle Cell Disease in India**

    2021

    JMIR mHealth and uHealth

    Kumar, R and Das, A

Sickle cell disease (SCD) is a chronic genetic disease that requires lifelong therapy and monitoring. Low drug adherence and poor monitoring may lead to an increase in morbidities and low quality of life. In the era of digital technology, various mobile health (mHealth) apps are being tested for their potential in increasing drug adherence in patients with SCD. We herewith discuss the applicability and feasibility of these mHealth apps for the management of SCD in India.

32. **Hydroxyurea and blood transfusion therapy for Sickle cell disease in South Asia: inconsistent treatment of a neglected disease**

    2021

    Orphanet Journal of Rare Diseases

    Darshana, T and Rees, D and Premawardhena, A

Background: Hydroxyurea and blood transfusion therapies remain the main therapeutic strategies for Sickle cell disease. Preliminary data suggest substantial variation and inconsistencies in practice of these two therapeutic modalities in South Asia. In this systematic review we searched Medline, Cochrane library and Scopus for articles on usage of hydroxyurea and blood transfusion therapies for sickle cell disease in South Asia published in English between October 2005 and October 2020. Results: We selected 41 papers: 33 from India, 3 from Sri Lanka, 2 each from Pakistan and Bangladesh and one from Nepal. Only 14 prospective trials focused on hydroxyurea therapy from which majority (n = 10; 71.4%) adopted fixed low dose (10Â mg/kg/day) regimen. With hydroxyurea therapy, 12 and 9 studies reported significant reductions in vaso-occlusive crises and transfusion requirement respectively. Severe anaemia (haemoglobin level < 6â€“7Â g/dl) was the commonest indicator (n = 8) for transfusion therapy followed by vaso-occlusive crisis. Conclusions: Published data on the hydroxyurea and transfusion therapies in South Asia are limited and heterogeneous. A clear gap of knowledge exists about the nature of the sickle cell disease in the Indian subcontinent particularly from countries outside India necessitating further evidence-based assessments and interventions.

33. **Implementation of indigenous electronic medical record system to facilitate care of sickle cell disease patients in chhattisgarh**

    2016

    Journal of Clinical and Diagnostic Research

    Choubey, M and Mishra, H and Soni, K and Patra, P K

Introduction: Sickle cell disease (SCD) is prevalent in central India including Chhattisgarh. Screening for SCD is being carried out by Government of Chhattisgarh. Electronic Medical Record (EMR) system was developed and implemented in two phases. Aim: Aim was to use informatics techniques and indigenously develop EMR system to improve the care of SCD patients in Chhattisgarh. EMR systems had to be developed to store and manage: i) huge data generated through state wide screening for SCD; ii) clinical data for SCD patients attending the outpatient department (OPD) of institute. Materials and Methods: â€˜State Wide Screening Data Interfaceâ€™ (SWSDI) was designed and implemented for storing and managing data generated through screening program. Further, â€˜Sickle Cell Patients Temporal Data Management Systemâ€™ (SCPTDMS) was developed and implemented for storing, managing and analysing sickle cell disease patientsâ€™ data at OPD. Both systems were developed using VB.Net and MS SQL Server 2012. Results: Till April 2015, SWSDI has data of 1294558 persons, out of which 121819 and 4087 persons are carriers and patients of sickle cell disease respectively. Similarly till June 2015, SCPTDMS has data of 3760 persons, of which 923 are sickle cell disease patients (SS) and 1355 are sickle cell carriers (AS). Conclusion: Both systems are proving to be useful in efficient storage, management and analysis of data for clinical and research purposes. The systems are an example of beneficial usage of medical informatics solutions for managing large data at community level.

34. Efficacy of fixed low dose hydroxyurea in Indian children with sickle cell anemia: A single centre experience

2013

Indian Pediatrics

Jain, D L and Apte, M and Colah, R and Sarathi, V and Desai, S and Gokhale, A and Bhandarwar, A and Jain, H L and Ghosh, K

Introduction: Data on the efficacy of hydroxyurea (HU) in Indian children with sickle cell anaemia (SCA) is limited. Hence, we have evaluated the efficacy of fixed low dose HU in Indian children. Methods: The study cohort consisted of 144 children (<18 years of age) with SCA having severe manifestations (â‰¥3 episodes of vasocclusive crisis or blood transfusions, or having â‰¥1 episode of acute chest syndrome or cerebrovascular stroke or sequestration crisis) who were started on fixed low dose HU (10 mg/kg/day). They were followed up for two years and monitored for the hematological and clinical efficacy and safety. Results: There was significant increase in the fetal hemoglobin level (HbF%), total hemoglobin and mean corpuscular volume. Vasoocclusive crises, blood transfusions, acute chest syndrome, sequestration crises and hospitalizations decreased significantly. Baseline HbF% had significant positive correlation with HbF% at 24 months. There was significant negative correlation between baseline HbF% and change in HbF% from baseline to 24 months. No significant correlation was found between HbF% at baseline and clinical event rates per year after HU. No major adverse events occurred during the study period. Conclusion: Fixed low dose HU is effective and safe in Indian children with SCA. Â© 2013 Indian Academy of Pediatrics.

35. Hydroxyurea in Sickle Cell Disease: Our Experience in Western India

2016

Indian Journal of Hematology and Blood Transfusion

Deshpande, S V and Bhatwadekar, S S and Desai, P and Bhavsar, T and Patel, A and Koranne, A and Mehta, A and Khadse, S

Sickle cell disease (SCD) is common in tribal belt of Gujarat, but not addressed effectively as it should be with effective use of Hydroxyurea, supportive care and counseling. In our single centre study of 70 patients of SCD who were only on Folic acid and Blood transfusion support, were analyzed and followed up for 1Â year in terms of their clinical symptoms, Blood transfusion requirement, laboratory parameters before and after Hydroxyurea therapy. We found statistically significant improvement in clinical symptoms and positive changes in laboratory parameters studied. This validates the well established role of Hydroxyurea in SCD as seen in the various international trials. Hence it is imperative that the well documented benefits of Hydroxyurea in various

International studies should be translated into clinical practice. SCD should be treated like a chronic disorder needing preventive therapy in form of Hydroxyurea and counseling with regular follow up.

36. Evolving locally appropriate models of care for Indian sickle cell disease

2016

Indian Journal of Medical Research

Serjeant, G R

The sickle cell gene in India represents a separate occurrence of the HbS mutations from those in Africa. Sickle cell disease in India occurs against different genetic and environmental backgrounds from those seen in African patients and there is evidence of clinical differences between the populations. Knowledge of the clinical features of African disease was drawn from the Jamaican Cohort Study, based on prospective follow up of all cases of sickle cell disease detected by the screening of 100,000 consecutive newborns in Kingston, Jamaica, and supplemented by observations from the Cooperative Study of Sickle Cell Disease in the US. Defining the principal causes of early morbidity in African sickle cell disease led to successful interventions including pneumococcal prophylaxis, parental education in the early diagnosis of acute splenic sequestration, and the early detection by trans-cranial Doppler of cerebral vessel stenosis predictive of stroke but their success depended on early diagnosis, ideally at birth. Although reducing mortality among patients with African forms of SS disease, the question remains whether these interventions are appropriate or justified in Indian patients. This dilemma is approached by comparing the available data in African and Indian forms of SS disease seeking to highlight the similarities and differences and to identify the deficiencies in knowledge of Indian disease. These deficiencies could be most readily addressed by cohort studies based on newborn screening and ince much of the morbidity of African disease occurs in the first five years of life, these need not be a daunting prospect for Indian health care personnel. Newborn screening programmes for sickle cell disease are already underway in India and appropriate protocols and therapeutic trials could quickly answer many of these questions. Without this knowledge, Indian physicians may continue to use possibly unnecessary and expensive models of care.

37. Low fixed-dose hydroxyurea in severely affected Indian children with sickle cell disease

2012

Hemoglobin

Jain, D L and Sarathi, V and Desai, S and Bhatnagar, M and Lodha, A

There is limited data on the efficacy of hydroxyurea (HU) in Indian sickle cell anemia patients who have severe manifestations despite high fetal hemoglobin (Hb F). Sixty sickle cell anemia children (518 years) with more than three episodes of vasoocclusive crises or blood transfusions per year were randomized to receive HU (n 30) or placebo (n 30) therapy. Fixed dose (10 mg/kg/day) of HU was administered for 18 months and the patients were followed-up monthly with clinical assessment and laboratory monitoring. In the HU group, hemoglobin (Hb) and Hb F levels increased significantly along with a significant decrease in the number of painful crises, blood transfusion requirements and hospitalizations compared to the placebo group. No major adverse events were observed in this study. In conclusion, low-fixed dose HU therapy was effective for the treatment of Indian sickle cell anemia children. However, there is a need for long-term studies to evaluate the efficacy and toxicity in a larger number of Indian sickle cell anemia patients. Â© 2012 Informa Healthcare USA, Inc.

38. Short term results of cementless total hip arthroplasty in sicklers.

2015

Indian Journal of Orthopaedics

Gulati, Yash and Sharma, Mrinal and Bharti, Bhupendra and Bahl, Vibhu and Bohra, Ishwar and Goswani, Amit

Background: Sickle cell (SC) disease leading to endarteritis induces skeletal changes in the form of osteitis, sclerosis of femoral canal and osteonecrosis of the femoral head. All these make total hip arthroplasty (THA) difficult and prolonged. There is increased risk of infection, SC crisis and increased complication rate. Our paper aims to highlight preoperative, intraoperative and postoperative hurdles encountered in performing THA in sicklers and the short term outcome using cementless implants. Materials and Methods: Thirty-nine patients with SC disease, who had osteonecrosis of the femoral head, were operated between 2007 and 2011. The mean age of patients was 22 years (range 13-49 years). There were twenty eight females and 11 males. Bilateral cementless total hip replacement (THR) was performed in 11 patients (22 hips) and in the rest unilateral (28 hips). Preoperative and postoperative modified Harris hip score was evaluated. The average followup was 3.8 years (range 2-6 years). Results: The average operating time was 96 min (range 88-148 min). The average blood loss was 880 ml (range 650-1200 ml). The average intraoperative blood transfused was 2.3 units (range 2-5 units). All patients showed an improvement in Harris hip score from 42 points preoperatively to 92 points at latest followup. Intraoperatively, one patient had a periprosthetic fracture. Six patients developed acute SC crisis and were managed in intensive care unit. Three patients developed wound hematoma. Three patients developed limb length discrepancy less than 1 cm. None had early or late dislocations, infection, heterotopic ossification, sciatic nerve palsy and aseptic loosening. Conclusion: THA in sicklers involves considerable challenge for the orthopedic surgeon. Management requires a multidisciplinary approach involving the anesthetist, hematologist and the orthopedic surgeon. Contrary to previous reports, THA in sicklers now has a predictable outcome especially with the use of cementless implants.

39. **Hydroxyurea responses in clinically varied beta, HbE-beta thalassaemia and sickle cell anaemia patients of Eastern India.**

    2018

    Annals of Hematology

    Chakravarty, Amit and Chatterjee, Tridip and Chakravarty, Sudipa

The haematological and clinical response to hydroxyurea was estimated in HbE-beta, beta thalassaemia and sickle cell anaemia patients of Eastern India, with variable clinical severity and transfusion requirement to determine whether hydroxyurea can help these patients to maintain their steady haemoglobin level without blood transfusions. Three hundred patients (189 HbE-beta thalassaemia, 95 beta thalassaemia and 16 other haemoglobinopathies including sickle cell anaemia) were selected for hydroxyurea therapy and were followed up for 48-60Â months. Results suggest significant response to hydroxyurea therapy in 19 beta and 99 HbE-beta patients in the transfusion-dependent group (GR-I). All of them became transfusion-independent while on hydroxyurea therapy. The majority of responding patients were IVS1-5(G-C) in one of their alleles in HbE-beta cases (83 out of 119). Though IVS1-5(G-C) was found to be the commonest mutation in our selected patients, the mutational background of the patients does not found to have any significant correlation with the response category towards hydroxyurea as per the results observed in our study. But, the drug works pretty well in most of the transfusion-dependent patients, as these patients were withdrawn from regular blood transfusion. At the same time, partial or no response to the drug hydroxyurea was also recorded in our study.

40. **Low dose hydroxyurea in children severely affected with sickle cell disease: hospital based randomized controlled study**

    American journal of hematology

    Jain, D

41. **Phytomedicines (medicines derived from plants) for sickle cell disease**

    2018

    Cochrane Database of Systematic Reviews

    Oniyangi, O and Cohall, D H

Abstract - Background Sickle cell disease, a common recessively inherited haemoglobin disorder, affects people from subâ€Saharan Africa, the Middle East, Mediterranean basin, Indian subcontinent, Caribbean and South America. It is associated with complications and a reduced life expectancy. Phytomedicines (medicine derived from plants in their original state) encompass many of the plant remedies from traditional healers which the populations most affected would encounter. Laboratory research and limited clinical trials have suggested positive effects of phytomedicines both in vivo and in vitro. However, there has been little systematic appraisal of their benefits. This is an update of a Cochrane Review first published in 2004, and updated in 2010, 2013, and 2015. Objectives To assess the benefits and risks of phytomedicines in people with sickle cell disease of all types, of any age, in any setting. Search methods We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register, the International Standard Randomised Controlled Trial Number Register (ISRCTN), the Allied and Complimentary Medicine Database (AMED), ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP). Dates of most recent searches: Cochrane Cystic Fibrosis and Genetic Disorders Haemoglobinopathies Trials Register: 10 April 2017; ISRCTN: 26 July 2017; AMED: 24 August 2017; ClinicalTrials.gov: 02 August 2017; and the WHO ICTRP: 27 July 2017. Selection criteria Randomised or quasiâ€randomised trials with participants of all ages with sickle cell disease, in all settings, comparing the administration of phytomedicines, by any mode to placebo or conventional treatment, including blood transfusion and hydroxyurea. Data collection and analysis Both authors independently assessed trial quality and extracted data. Main results Two trials (182 participants) and two phytomedicines Niprisan Â® (also known as Nicosan Â®) and Ciklavit Â® were included. The Phase IIB (pivotal) trial suggests that Niprisan Â® was effective in reducing episodes of severe painful sickle cell disease crisis over a sixâ€month period (lowâ€quality evidence). It did not affect the risk of severe complications or the level of anaemia (lowâ€quality evidence). No serious adverse effects were reported. The single trial of Cajanus cajan (Ciklavit Â®) reported a possible benefit to individuals with painful crises (lowâ€quality evidence), and a possible adverse effect (nonâ€significant) on the level of anaemia (lowâ€quality evidence). Authors' conclusions While Niprisan Â® appeared to be safe and effective in reducing severe painful crises over a sixâ€month followâ€up period, further trials are required to assess its role in the management of people with sickle cell disease and the results of its multicentre trials are awaited. Currently no conclusions can be made regarding the efficacy of Ciklavit Â® . Based on the published results for Niprisan Â® and in view of the limitations in data collection and analysis of both trials, phytomedicines may have a potential beneficial effect in reducing painful crises in sickle cell disease. This needs to be further validated in future trials. More trials are required on the safety and efficacy of phytomedicines used in managing sickle cell disease. Plain language summary Phytomedicines (medicines derived from plants) for sickle cell disease Review question We reviewed the evidence about the effect and safety of phytomedicines in people with sickle cell disease of all types, of any age, in any setting. Background Sickle cell disease is an inherited blood condition caused by defects in the production of haemoglobin. Haemoglobin is the part of the red blood cell that carries oxygen across the body. Sickle cell disease occurs when people inherit faulty genes responsible for producing haemoglobin from both parents. A variety of complications and a reduced life expectancy are linked with sickle cell disease. Phytomedicines are medicines derived from plants in their original state. People with sickle cell disease may come across them in terms of plantâ€remedies from traditional healers. Their benefits have not been evaluated systematically. Laboratory work has long suggested that these medicines may help to ease the symptoms of sickle cell disease. Search date The evidence is current to: 24 August 2017. Study characteristics Two trials (182 participants) and two phytomedicines Niprisan Â® (also known as Nicosan Â®) and Ciklavit Â® were included. Key results This review found that Niprisan Â® may help to reduce episodes of sickle cell disease crises associated with severe pain. Ciklavit Â® , which has been reported to reduce painful crises in people with sickle cell disease, deserves further study before recommendations can be made regarding its use. The trial of Ciklavit Â® also reported a possible adverse effect on the level of anaemia. Both formulations reported no serious adverse symptoms or derangement of liver or kidney function in the participants. More detailed and larger trials of these medicines will need to be carried out before we can make any recommendations about their use. Further research should also assess longâ€term outcome measures. Quality of the evidence We judged the quality of the evidence from this review to be of low to very low quality, depending on the outcome measured.

42. Nonâ€surgical interventions for treating heavy menstrual bleeding (menorrhagia) in women with bleeding disorders

2016

Cochrane Database of Systematic Reviews

Ray, S and Ray, A

Abstract - Background Heavy menstrual bleeding without an organic lesion is mainly due to an imbalance of the various hormones which have a regulatory effect on the menstrual cycle. Another cause of heavy menstrual bleeding with no pelvic pathology, is the presence of an acquired or inherited bleeding disorder. The haemostatic system has a central role in controlling the amount and the duration of menstrual bleeding, thus abnormally prolonged or profuse bleeding does occur in most women affected by bleeding disorders. Whereas irregular, preâ€menarchal or postâ€menopausal uterine bleeding is unusual in inherited or acquired haemorrhagic disorders, severe acute bleeding and heavy menstrual bleeding at menarche and chronic heavy menstrual bleeding during the entire reproductive life are common. This is an update of a previously published Cochrane Review. Objectives To determine the efficacy and safety of nonâ€surgical interventions versus each other, placebo or no treatment for reducing menstrual blood loss in women with bleeding disorders. Search methods We searched the Cochrane Cystic Fibrosis Haemoglobinopathies Trials Register (25 August 2016), Embase (May 2013), LILACS (February 2013) and the WHO International Clinical Trial registry (February 2013). Selection criteria Randomised controlled studies of nonâ€surgical interventions for treating heavy menstrual bleeding (menorrhagia) in women of reproductive age suffering from a congenital or acquired bleeding disorder. Data collection and analysis Two authors independently assessed studies for inclusion, extracted data and assessed the risk of bias. Main results Three crossâ€over studies, with 175 women were included in the review. All three studies had an unclear risk of bias with regards to trial design and overall, the quality of evidence generated was judged to be poor. Two of the studies (n = 59) compared desmopressin (1â€deaminoâ€8â€Dâ€arginine vasopressin) with placebo. Menstrual blood loss was the primary outcome for both of these studies. Neither study found clear evidence of a difference between groups. The first of these reported a mean difference in menstrual blood loss in the desmopressin versus placebo group of 21.20 mL (95% confidence interval â€19.00 to 61.50) The second study reported that even though there was an improvement of pictorial bleeding assessment chart scores with desmopressin and placebo when compared to pretreatment assessment, there was no clear evidence of difference in these scores when the two were compared to each other (results presented graphically, P = 0.51). The data from these studies could not be combined. The third study (n = 116) compared desmopressin with tranexamic acid (n = 116). This study found a decrease in pictorial bleeding assessment chart scores after both treatments as compared to baseline. The decrease in these scores was greater for tranexamic acid than for desmopressin, with a mean difference of 41.6 mL (95% confidence interval 19.6 to 63) (P < 0.0002). In relation to adverse events, across two studies, there was no clear evidence of a difference when placebo was compared to desmopressin, risk ratio 1.17 (95% confidence interval 0.41 to 3.34) . The same was also true when desmopressin was compared to tranexamic acid, risk ratio 1.17 (95% confidence interval 0.41 to 3.34). Only the study that compared desmopressin to tranexamic acid assessed quality of life. However, we are unable to present any data from this study, since no differences in this outcome between the two intervention groups were reported. Authors' conclusions Evidence from randomised controlled studies on the effect of desmopressin when compared to placebo in reducing menstrual blood loss is very limited and inconclusive. Two studies, each with a very limited number of participants, have shown uncertain effects in menstrual blood loss and adverse effects. A nonâ€randomised comparison in one of the studies points to the value of combining desmopressin and tranexamic acid, which needs to be tested in a formal randomised controlled study comparison. When tranexamic acid was compared to desmopressin, a single study showed a reduction in menstrual blood loss with tranexamic acid use compared to desmopressin. There is a need to evaluate nonâ€surgical methods for treating of menorrhagia in women with bleeding disorders through randomised controlled studies. Such methods would be more acceptable than surgery for women wishing to retain their fertility. Given that women may need to use these treatments throughout their entire reproductive life, longâ€term sideâ€effects should be evaluated. Plain language summary Medical therapies for treating heavy menstrual bleeding in women with bleeding disorders Review question We reviewed

the evidence about the effect and safety of nonâ€surgical treatments versus each other, placebo or no treatment for reducing menstrual blood loss in women with bleeding disorders. This is an update of a previously published Cochrane Review. Background Heavy menstrual bleeding is one of the most common symptoms in women with bleeding disorders. A sizeable population of women with heavy menstrual bleeding are affected by either inherited or acquired bleeding disorders and at the time of presentation these women are considerably younger than the women who suffer from this due to other reasons. Since heavy menstrual bleeding starts at the very onset of menarche and continues throughout reproductive life, the quality of life of these women is severely affected and they are at an increased risk of developing ironâ€deficiency anaemia. Search date The evidence is current to: 25 August 2016. Study characteristics The review included three studies on nonâ€surgical treatments in 175 women with a bleeding disorder who were experiencing heavy menstrual bleeding . Two s tudies compared desmopressin to placebo and one study compared desmopressin to tranexamic acid. The women included in the studies were selected for one treatment or the other randomly. The studies lasted from two to four months. Key results Two studies of the three studies (with a total of 59 women) found no clear evidence of a difference in desmopressin (1â€deaminoâ€8â€Dâ€arginine vasopressin) in reducing menstrual blood loss when compared to placebo. One of these studies continued with an open nonâ€randomised comparison of a combination of desmopressin with tranexamic acid versus placebo and found a significant reduction in menstrual blood loss. However, the nonâ€randomised design of this comparison is an additional potential source of bias. The third study (116 women), which had more participants than the other two studies combined, found a greater reduction in menstrual blood loss with tranexamic acid use than with desmopressin. We were unable to present any data on quality of life from this study, since no differences in between the two intervention groups were reported. There was no clear evidence of difference in the risk of side effects with desmopressin as compared to tranexamic acid. None of the studies dealt with cost effectiveness. Quality of the evidence We were not able to adequately assess the studies in relation to how the women were allocated to the treatment groups and we judged the overall quality of the evidence as poor.

43. Drugs for preventing red blood cell dehydration in people with sickle cell disease

2018

Cochrane Database of Systematic Reviews

Nagalla, S and Ballas, S K

Abstract - Background Sickle cell disease is an inherited disorder of hemoglobin, resulting in abnormal red blood cells. These are rigid and may block blood vessels leading to acute painful crises and other complications. Recent research has focused on therapies to rehydrate the sickled cells by reducing the loss of water and ions from them. Little is known about the effectiveness and safety of such drugs. This is an updated version of a previously published review. Objectives To assess the relative risks and benefits of drugs to rehydrate sickled red blood cells. Search methods We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register. We also searched online trials registries for any ongoing trials (01 July 2018). Last search of the Group's Haemoglobinopathies Trials Register: 08 October 2018. Selection criteria Randomized or quasiâ€randomized controlled trials of drugs to rehydrate sickled red blood cells compared to placebo or an alternative treatment. Data collection and analysis Both authors independently selected studies for inclusion, assessed study quality and extracted data. Main results Of the 51 studies identified, three met the inclusion criteria, including 524 people with sickle cell disease aged between 12 and 65 years of age. One study tested the effectiveness of zinc sulphate as compared to placebo and the remaining two assessed senicapoc versus placebo. No deaths were seen in any of the studies (lowâ€quality evidence). The zinc sulphate study showed a significant reduction in painful crises (in a total of 145 participants) over one and a half years, mean difference â€2.83 (95% confidence interval â€3.51 to â€2.15) (moderateâ€quality evidence). However, analysis was restricted due to limited statistical data. Changes to red blood cell parameters and blood counts were inconsistent (very lowâ€quality evidence). No serious adverse events were noted in the study. The Phase II doseâ€finding study of senicapoc (a Gardos channel blocker) compared to placebo showed that the high dose senicapoc showed significant improvement in change in hemoglobin level, the number and proportion of dense red blood cells, red

blood cell count and indices and hematocrit value (very lowâ€quality evidence). The results with lowâ€dose senicapoc were similar to the highâ€dose senicapoc group but of lesser magnitude. There was no difference in the frequency of painful crises between the three groups (lowâ€quality evidence). A subsequent Phase III study of senicapoc was terminated early since there was no difference observed between the treatment and control groups in the primary end point of painful crises. Authors' conclusions While the results of zinc for reducing sickleâ€related crises are encouraging, larger and longerâ€term multicenter studies are needed to evaluate the effectiveness of this therapy for people with sickle cell disease. While the Phase II and the prematurely terminated phase III studies of senicapoc showed that the drug improved red blood cell survival (depending on dose), this did not lead to fewer painful crises. Given this is no longer an active area of research, this review will no longer be regularly updated. Plain language summary Drugs that aim to reduce the loss of water from red blood cells in people with sickle cell disease Review question We reviewed the evidence to assess the relative risks and benefits of drugs to rehydrate sickled red blood cells. Background Sickle cell disease is an inherited condition that causes red blood cells to become sickle shaped when they lose water. This leads to a high risk of the blood vessels becoming blocked. Such blockages can cause pain, stroke and damage to organs. Recent therapies aim to stop the cells becoming sickle shaped by preventing them losing water. Search date The evidence is current to: 08 October 2018. Study characteristics The review included three studies with 524 people with sickle cell disease aged between 12 and 65 years of age. The intervention in one study was zinc sulphate and in two studies was senicapoc. Each study was compared to a placebo group (a substance which contains no medication). For each study people were selected for one treatment or the other randomly. The studies lasted from three months to 18 months. Key results The study with zinc sulphate showed that this drug may be able to reduce the number of sickle cell crises without causing toxic effects (lowâ€quality evidence). There were 145 participants in this study and results showed a significant reduction in the total number of serious sickleâ€related crises over one and a half years, mean difference â€2.83 (95% confidence interval â€3.51 to â€2.15) (moderateâ€quality evidence). However, our analysis was limited since not all data were reported. Changes to red blood cell measurements and blood counts were not consistent (very lowâ€quality evidence). No serious adverse events were noted in the study. The two studies with senicapoc demonstrated that this drug increases the red blood survival and has a role in preventing red blood cell dehydration in people with sickle cell disease (very lowâ€quality evidence). The higher dose of the drug was more effective compared to the lower dose. But these changes in the red blood cells did not translate into positive clinical outcomes in terms of reduction in the number of sickle cell crises (lowâ€quality evidence). Senicapoc had a favourable safety profile. More longerâ€term research is needed on these drugs and others that might prevent water loss in red blood cells. Given this is no longer an active area of research, this review will no longer be regularly updated. Quality of the evidence The quality of the evidence was mixed across outcomes.

44. Management of sickle cell disease in the community

2014

BMJ : British Medical Journal (Online)

Brousse, Valentine and Makani, Julie and Rees, David C

Summary points All children with sickle cell disease should take penicillin twice a day until 5 years of age at least Acute neurological symptoms in children and adults with sickle cell disease necessitate urgent referral to hospital All patients should receive annual vaccination against influenza and other appropriate vaccinations where available Patients living in most parts of Africa should use insecticide treated bed nets and take malarial prophylaxis Children with severe types of sickle cell disease (HbSS and HbS/[beta]0 thalassaemia) should be offered primary stroke prevention with annual transcranial Doppler scans and blood transfusion when resources allow this Children and adults should be offered treatment with hydroxyurea if they have two or more episodes of severe acute pain in a year, or acute chest syndrome Children, families, and adults should be offered education about sickle cell disease and managing its complications Sickle cell disease is characterised by unpredictable episodes of acute illness, progressive organ damage, and a lack of effective treatments. If two or more episodes occur, splenectomy is often recommended, on the basis of case series that show a high rate of recurrence. 25 Parvovirus B19 infection causes slapped cheek syndrome and also infects erythroid cells, causing transient

reticulocytopenia, which last about a week. Because sickled red cells have a shorter survival time than normal ones, reticulocytopenia can result in severe anaemia requiring blood transfusion, with recovery occurring after about seven days. 26 Increased anaemia can also be associated with folate and iron deficiency, and renal impairment, although this is usually of gradual onset. Tips for non-specialists Sickle cell disease is very variable, with some patients having severe symptoms every month and others being largely asymptomatic Encourage adherence to penicillin prophylaxis whenever possible, and facilitate this by providing appropriate access to repeat prescriptions Ensure that all patients receive recommended vaccines, including annual vaccination against influenza in many countries Many episodes of uncomplicated acute pain can be managed at home with simple analgesia and community support Ensure children and adults who were born overseas in high prevalence countries are offered haemoglobinopathy screening (full blood count, haemoglobin analysis) Additional educational resources Resources for healthcare professionals National Heart, Lung and Blood Institute (www.nhlbi.nih.gov/health/prof/blood/sickle/sc_mngt.pdf)-American website with information on diagnosis and management of all aspects of sickle cell disease for high-income countries; free resource, no registration NHS Sickle Cell and Thalassaemia Screening Programme (www.sct.screening.nhs.uk)-Information on antenatal and neonatal haemoglobinopathy screening in England, with guidelines and standards on diagnosis, clinical management, and patient information leaflets; free, no registration. Global Sickle Cell Disease Network (www.globalsicklecelldisease.org)-Information on sickle cell centres and meetings across the world, with names of sickle cell disease specialists across the world; free, registration for full access South Thames Sickle Cell and Thalassaemia Network (www.ststn.co.uk)-Information on meetings, and access to guidelines covering diagnosis and management; free, no registration Resources for patients Sickle Cell Society (www.sicklecellsociety.org)-Website of UK Sickle Cell Society with news, information, and patient leaflets; free, no registration NHS choices (www.nhs.uk/conditions/Sickle-cell-anaemia/Pages/Introduction.aspx)-Patient information on NHS screening programme for sickle cell disease; free, no registration Sickle Cell Disease Association of America (www.sicklecelldisease.org)-American website with news, guidelines, and information; free, no registration Rofsed (www.rofsed.fr)-French language website for children, parents, and professionals; particularly good for teenagers; free, no registration Areas for future research The value of aggressively treating all children with sickle cell disease with interventions such as hydroxyurea, regular blood transfusion, or haematopoietic stem cell transplantation to prevent organ damage and premature death The value of simple commonly used interventions during acute admissions, including intravenous fluids, oxygen, thromboprophylaxis, and antibiotics The development of specific treatments to shorten the length and severity of acute vaso-occlusive pain The discovery and development of drugs designed to treat sickle cell disease, including those that promote haemoglobin F synthesis, prevent red cell dehydration, and inhibit HbS polymerisation The validation of DNA, plasma, and imaging biomarkers that can identify infants at risk of severe complications early The development of evidence based interventions in low and middle income countries, particularly African and Asian ones Penny Ryba reviewed and commented on the article.

45. Effect of Poloxamer 188 vs Placebo on Painful Vaso-Occlusive Episodes in Children and Adults With Sickle Cell Disease: A Randomized Clinical Trial: The Journal of the American Medical Association

2021

JAMA

Casella MD, James F and Barton PhD, Bruce A and Kanter MD, Julie and Black MD, MSc, L Vandy and Majumdar MD, Suvankar and Inati MD, Adlette and Wali MD, Yasser and Drachtman MD, Richard A and Abboud MD, Miguel R and Kilinc MD, Yurdanur and Fuh MD, Beng R and Al-Khabori MD, Murtadha K and Takemoto MD, Clifford M and Salman MD, Emad and Sarnaik MD, Sharada A and Shah MD, Nirmish and Morris MD, Claudia R and Keates-Baleeiro MD, Jennifer and Raj MD, Ashok and Alvarez MD, Ofelia A and Hsu MD, PhD, Lewis L and Thompson MD, MPH, Alexis A and Sisler MD, India Y and Pace MD, Betty S and Noronha MD, Suzie A and Lasky III, MD, Joseph L and de Julian MD, MSc, PhD, Elena Cela and Godder MD, Kamar and Thornburg MD, MS, Courtney Dawn and Kamberos DO, Natalie L and Nuss MD, Rachelle and Marsh MD, Anne M and Owen MD, William C and Schaefer MD, Anne and

Tebbi MD, Cameron K and Chantrain MD, PhD, Christophe F and Cohen MD, Debra E and Karakas MD, Zeynep and Piccone MD, Connie M and George MD, Alex and Fixler MD, Jason M and Singleton MD, Tammuella C and Moulton MD, Thomas and Quinn MD, MS, Charles T and Lobo MD, PhD, Clarisse Lopes de Castro and Almomen MD, Abdulkareem M and Goyal-Khemka MD, Meenakshi and Maes MD, Philip and Emanuele PhD, MBA, Marty and Gorney MS, Rebecca T and Padgett PhD, Claire S and Parsley DO, Ed and Kronsberg MS, Shari S and Kato MD, Gregory J and Gladwin MD, Mark T and Casella, J F and Barton, B A and Kanter, J and Black, L V and Majumdar, S and Inati, A and Wali, Y and Drachtman, R A and Abboud, M R and Kilinc, Y and Fuh, B R and Al-Khabori, M K and Takemoto, C M and Salman, E and Sarnaik, S A and Shah, N and Morris, C R and Keates-Baleeiro, J and Raj, A and Alvarez, O A and Hsu, L L and Thompson, A A and Sisler, I Y and Pace, B S and Noronha, S A and Lasky, J L and De Julian, E C and Godder, K and Thornburg, C D and Kamberos, N L and Nuss, R and Marsh, A M and Owen, W C and Schaefer, A and Tebbi, C K and Chantrain, C F and Cohen, D E and Karakas, Z and Piccone, C M and George, A and Fixler, J M and Singleton, T C and Moulton, T and Quinn, C T and De Castro Lobo, C L and Almomen, A M and Goyal-Khemka, M and Maes, P and Emanuele, M and Gorney, R T and Padgett, C S and Parsley, E and Kronsberg, S S and Kato, G J and Gladwin, M T and Casella MD, James F and Barton PhD, Bruce A and Kanter MD, Julie and Black MD, MSc, L Vandy and Majumdar MD, Suvankar and Inati MD, Adlette and Wali MD, Yasser and Drachtman MD, Richard A and Abboud MD, Miguel R and Kilinc MD, Yurdanur and Fuh MD, Beng R and Al-Khabori MD, Murtadha K and Takemoto MD, Clifford M and Salman MD, Emad and Sarnaik MD, Sharada A and Shah MD, Nirmish and Morris MD, Claudia R and Keates-Baleeiro MD, Jennifer and Raj MD, Ashok and Alvarez MD, Ofelia A and Hsu MD, PhD, Lewis L and Thompson MD, MPH, Alexis A and Sisler MD, India Y and Pace MD, Betty S and Noronha MD, Suzie A and Lasky III, MD, Joseph L and de Julian MD, MSc, PhD, Elena Cela and Godder MD, Kamar and Thornburg MD, MS, Courtney Dawn and Kamberos DO, Natalie L and Nuss MD, Rachelle and Marsh MD, Anne M and Owen MD, William C and Schaefer MD, Anne and Tebbi MD, Cameron K and Chantrain MD, PhD, Christophe F and Cohen MD, Debra E and Karakas MD, Zeynep and Piccone MD, Connie M and George MD, Alex and Fixler MD, Jason M and Singleton MD, Tammuella C and Moulton MD, Thomas and Quinn MD, MS, Charles T and Lobo MD, PhD, Clarisse Lopes de Castro and Almomen MD, Abdulkareem M and Goyal-Khemka MD, Meenakshi and Maes MD, Philip and Emanuele PhD, MBA, Marty and Gorney MS, Rebecca T and Padgett PhD, Claire S and Parsley DO, Ed and Kronsberg MS, Shari S and Kato MD, Gregory J and Gladwin MD, Mark T

Importance Although effective agents are available to prevent painful vaso-occlusive episodes of sickle cell disease (SCD), there are no disease-modifying therapies for ongoing painful vaso-occlusive episodes; treatment remains supportive. A previous phase 3 trial of poloxamer 188 reported shortened duration of painful vaso-occlusive episodes in SCD, particularly in children and participants treated with hydroxyurea. Objective To reassess the efficacy of poloxamer 188 for vaso-occlusive episodes. Design, Setting, and Participants Phase 3, randomized, double-blind, placebo-controlled, multicenter, international trial conducted from May 2013 to February 2016 that included 66 hospitals in 12 countries and 60 cities; 388 individuals with SCD (hemoglobin SS, SC, S-Î²0 thalassemia, or S-Î²+ thalassemia disease) aged 4 to 65 years with acute moderate to severe pain typical of painful vaso-occlusive episodes requiring hospitalization were included. Interventions A 1-hour 100-mg/kg loading dose of poloxamer 188 intravenously followed by a 12-hour to 48-hour 30-mg/kg/h continuous infusion (nâ€‰=â€‰194) or placebo (nâ€‰=â€‰194). Main Outcomes and Measures Time in hours from randomization to the last dose of parenteral opioids among all participants and among those younger than 16 years as a separate subgroup. Results Of 437 participants assessed for eligibility, 388 were randomized (mean age, 15.2 years; 176 [45.4%] female), the primary outcome was available for 384 (99.0%), 15-day follow-up contacts were available for 357 (92.0%), and 30-day follow-up contacts were available for 368 (94.8%). There was no significant difference between the groups for the mean time to last dose of parenteral opioids (81.8 h for the poloxamer 188 group vs 77.8 h for the placebo group; difference, 4.0 h [95% CI, â^'7.8 to 15.7]; geometric mean ratio, 1.2 [95% CI, 1.0-1.5]; Pâ€‰=â€‰.09). Based on a significant interaction of age and treatment (Pâ€‰=â€‰.01), there was a treatment difference in time from randomization to last administration of parenteral opioids for participants younger than 16 years (88.7 h in the poloxamer 188 group vs 71.9 h in the placebo group; difference, 16.8 h [95% CI, 1.7-32.0]; geometric mean ratio, 1.4 [95% CI, 1.1-1.8]; Pâ€‰=â€‰.008). Adverse events that were more common in the poloxamer 188 group than the placebo group included hyperbilirubinemia (12.7% vs 5.2%); those

more common in the placebo group included hypoxia (12.0% vs 5.3%). Conclusions and Relevance Among children and adults with SCD, poloxamer 188 did not significantly shorten time to last dose of parenteral opioids during vaso-occlusive episodes. These findings do not support the use of poloxamer 188 for vaso-occlusive episodes.

46. Hydroxyurea in sickle cell disease-A study of clinico-pharmacological efficacy in the Indian haplotype

2009

Blood Cells, Molecules, and Diseases

Italia, K and Jain, D and Gattani, S and Jijina, F and Nadkarni, A and Sawant, P and Nair, S and Mohanty, D and Ghosh, K and Colah, R and Italia K, Jain D Gattani S Jijina F Nadkarni A Sawant P Nair S Mohanty D Ghosh K and Colah, R and Italia, K and Jain, D and Gattani, S and Jijina, F and Nadkarni, A and Sawant, P and Nair, S and Mohanty, D and Ghosh, K and Colah, R and Italia K, Jain D Gattani S Jijina F Nadkarni A Sawant P Nair S Mohanty D Ghosh K and Colah, R

There is clinical variability in the presentation of sickle cell disease among Indians. Vaso-occlusive crisis is common among non-tribal patients. Hydroxyurea, induces fetal hemoglobin (HbF) synthesis and reduces the clinical severity of sickle cell disease but individual patients have a variable response. This study was undertaken to investigate the efficacy and safety of hydroxyurea in Indians with severe manifestations where the Î²s gene is linked to the Arab-Indian haplotype and is associated with higher HbF levels. Seventy-seven patients (29 adult sickle homozygous, 25 pediatric sickle homozygous, 23 adult sickle Î²-thalassemia) selected for hydroxyurea therapy were evaluated for clinical, hematological, biochemical and genetic parameters and were followed for 24 months. Ninety-eight point seven percent of the sickle chromosomes were linked to the Arab-Indian haplotype, 27% of patients had associated Î± thalassemia and 65% were Xmn I +/+. Seventy-eight percent of the patients had no further crises after starting hydroxyurea. This effect was accompanied by a significant increase in HbF ($p < 0.001$), but this increase was variable in individual cases. There was also an increase in Î³ gene mRNA expression in the few cases so studied. Hemoglobin levels increased significantly ($p < 0.001$) resulting in the cessation of blood transfusions. Leucopoenia was observed in one patient. Hydroxyurea was effective in reducing the clinical severity in Indian patients who initially had higher HbF levels and the presence of ameliorating factors, such as Î±-thalassemia and the Xmn I polymorphism. Hydroxyurea therapy with careful monitoring can thus change the quality of life of Indians with sickle cell disease. Â© 2008 Elsevier Inc. All rights reserved.

47. Study of twenty one cases of red cell exchange in a tertiary care hospital in Southern India

2016

Journal of Clinical and Diagnostic Research

Daniel, M Joshua and Muddegowda, Prakash H and Chezhiansubash and Lingegowda, Jyothi B and Gopal, Niranjan and Prasad, Krishna and Joshua Daniel, M and Muddegowda, Prakash H and Subash, C and Lingegowda, Jyothi B and Gopal, Niranjan and Prasad, Krishna and Daniel, M Joshua and Muddegowda, Prakash H and Chezhiansubash and Lingegowda, Jyothi B and Gopal, Niranjan and Prasad, Krishna

Introduction: Red Cell Exchange (RCE) is removal of a patientâ€™s red blood cells while replacing with donor red blood cells either manually or using automated systems. RCE is beneficial in patients with Sickle Cell Disease (SCD) either during sickling crisis or prior to major surgical procedures to bring down the sickling percentage as high sickling percentage during prolonged anaesthesia may lead to vaso-occlusive crisis. It is also employed in patients infested with malaria and babesiosis where parasitic index remain high despite medical management. RCE is also tried as an adjuvant therapy in certain poisons like nitrobenzene and carbon monoxide when first line management fails. Aim: To study the effectiveness, clinical outcome, challenges and complications of RCE in various clinical scenario and to understand how this procedure can be effectively utilized in the management of patients in Indian scenario. Materials and Methods: This retro prospective study was conducted in tertiary care

center in southern India which analyzed 21 RCE procedures performed on patients with different clinical conditions. Of the 21 RCE performed, 18 procedures were performed on patients with case of sickle cell disease, Two procedures were performed on patients infested with severe falciparum malaria and one procedure was performed on a patient with nitrobenzene poisoning. All procedures were performed using Spectra OptiaÂ® Apheresis System-Terumo BCT. Results: All the 18 patients who underwent the RCE for sickle cell anaemia were admitted for hemi-arthroplasty for avascular necrosis of the head of femur. The average initial HbS levels were between 73-85% and post RCE it was brought down to 22-29% and was achieved in a single sitting in all the cases. Among the two patients infested with severe falciparum malaria, RCE helped in reducing the infestation rate. In case of nitrobenzene poisoning, RCE helped in improvement of oxygen saturation and patient showed significant improvement. Conclusion: RCE is a safe and clinically effective therapeutic modality with very minimal to nil side effects. RCE is possibly underutilized therapy in developing world like India due to various reasons like inadequate awareness/ technical expertise, lack of equipments and facilities to identify the clinical conditions per se etc.

48. **Efficacy of zinc therapy in prevention of crisis in sickle cell anemia: a double blind, randomized controlled clinical trial.**

    1995

The Journal of the Association of Physicians of India

Gupta, V L and Chaubey, B S and VL, Gupta and Chaubey, B S

145 patients were recruited in the trial while 130 completed it. Patients were randomized to receive zinc sulphate capsules. 220 mgm three times a day or identical placebo. Major outcome variable was 'Sickle cell crisis'. After a follow up of 1.5 years, the mean number of episodes of crisis was 2.46 +/- 1.04 in the intervention group and 5.29 +/- 2.58 in the control group ($p < 0.025$; 95% CI for difference between groups: 1.98, 3.42). Mean duration of hospital stay was 4.3 +/- 2.2 days in the intervention group and 3.9 +/- 1.6 days in the control group. The difference was not significant ($p > 0.05$). There was a significant reduction of the mean number of infective episodes and associated morbidity in patients with sickle cell anaemia.

49. **Continuous intravenous infusion vs intermittent intramuscular injection of tramadol for sickle cell vasoocclusive crisis: an open label randomized trial**

    2020

    Indian journal of hematology & blood transfusion

    BP, Kar and Mohanty, P K and Kar, B P and Mohanty, P K and BP, Kar and Mohanty, P K

Aims & Objectives: Sickle cell disease is a global health problem and in India it is prevalent in Gujarat, Maharashtra, Madhya Pradesh, Chhattisgarh, Odisha and Jharkhand. The protean manifestation as vaso occlusive crisis occurs repeatedly and cumbersome to manage and responsive for increased morbidity and mortality. Inadequately managed pain have negative consequences in physiological functions such as autonomic hyperactivity and reduced motility leading to muscle wasting, joint stiffening and decalcification with deleterious psychological changes. As per WHO Analgesic ladder for mild to moderate pain long acting opioid or continuous infusion short acting opioid is required with/without non opioid adjuvant agents. Tramadol is a synthetic codeine analogue which is weak mu opioid receptor agonist. Usual practice is to administer Tramadol intermittently as intramuscular injection which results in breakthrough pain. Ideal way is to infusion, which is not in usual practice. Patients/Materials & Methods: The study conducted after Ethical approval and CTRI registration on indoor patients of VIMSAR, Burla with diagnosed case of sickle cell disease having VOC defined as pain involving skeleton, chest, abdomen or all three lasting four hours or more. Study groups were randomly divided either getting Tramadol infusion or intermittent intramuscular injection and monitored four hourly for assessment of pain on visual analogue scale and for breakthrough pain in which adjuvant analgesic Inj Ketorolac/Diclofenac used. Results: We found in the study that the mean duration of hospital stay, better pain relief, lesser amount of

breakthrough pain and lesser cumulative dose of Tramadol in continuous intravenous infusion group compared to the intermittent intramuscular group. Discussion & Conclusion: In sickle cell disease vaso occlusive crisis patient appropriate pain assessment and adequate pain management is considered to be standard of care. Given its profound impact in patient physiology and quality of life, the management of pain must be an important in therapeutic intervention. Although Morphine is the most ideal opioid recommended for painful crisis, use is limited due to regulatory prohibition along with Codeine, Oxycodone and Hydromorphone which are not available. Tramadol is as effective as Morphine in mild to moderate pain and ideal way is to use intravenous infusion.

50. Haemorheological treatment of painful sickle cell crises. Use of pentoxifylline.

1991

The Journal of the Association of Physicians of India

Poflee, V W and Gupta, O P and Jain, A P and Jajoo, U N and Poflee VW, Gupta O P Jain A P and Jajoo, U N and Poflee, V W and Gupta, O P and Jain, A P and Jajoo, U N

A variety of drugs have been tried, with little or no benefit, to prevent and treat painful crises in patients with sickle cell anaemia. The new drug pentoxifylline, which has the ability to alter red cell flexibility, was tried in nine patients with painful vaso-occlusive crises. Another nine matched patients served as control. While no patient in the control group improved, five patients in the pentoxifylline group responded favourably within 48 hours. We conclude that pentoxifylline may be useful in patients with acute painful vasoocclusive crises due to sickle cell anaemia.

51. Therapeutic red cell exchange in malaria and sickle cell disease

2013

Vox Sanguinis

Deshpande, A S and Kalgutkar, S and Sawant, R

Background: Therapeutic red cell exchange has been used successfully over the past few years, in a variety of clinical conditions as a therapeutic modality. The indications range from infectious diseases like malaria and hemoglobinopathies like sickle cell disease. Aims: To review procedural parameters and clinical efficacy of Therapeutic Erythrocytapheresis (TEA) procedures carried out in a Tertiary care multi-speciality hospital. Methods: Two children (aged 12 years & 10 years) with severe falciparum malaria having Infestation rate (IR) >50% and multi organ failure, one adult patient and two pediatric patients of SCD in crisis were subjected to therapeutic red cell exchange procedure using cell separator (Cobe Spectra). Critical factors like type of vascular access, anticoagulant to be used, volume of red cell to be removed, replacement fluid to be used, etc were decided before starting the procedure. The treatment plan was to reduce the number of infected/defective red blood cells, maintain or alter the patient's hematocrit and control the fluid balance. Results: One volume RBC exchange using RBC units with Hct >55% & blood priming in pediatric patients were performed. Average procedure time was 70 min and all procedures were uneventful. TEA (1 procedure per patient) carried out for two children suffering from severe malaria showed a decrease in infestation rate (IR) from 75% to 18% in the first case and from 67% to 8% in the second case post procedure. Hb increased from 7 gm/dl to 10 gm/dl in the first case and from 5 gm/dl to 8.9 gm/dl in the second case. TEA carried out for the adult patient in sickle cell crisis (three exchange procedures over a period of 1 year at 4 monthly interval) showed a reduction in HbS level from >60% to <20% post procedure after every exchange. Hematocrit was maintained at 30% after each exchange procedure. TEA carried out for pediatric patient in sickle cell crisis showed a drop in HbS from 71% to 14% & in the second case from 77% to 31% post procedure. Conclusion: TREX with automated cell separators resulted in rapid correction of anemia, a rapid decrease in infected/ defective red cells and improvement in patients clinical condition. It is more effective, less time consuming and offers a rapid adjunctive therapy to treat severe cases of Malaria & SCD and can be safely used even in children.

52. Balancing cure versus toxicity-haematopoietic stem cell transplantation for sickle cell anemia

2018

Indian Journal of Hematology and Blood Transfusion

Nikila, R and Patel, S and Sankaran, M and Venkateswaran, V S and Kesavan, M R and Uppuluri, R and Revathi, R and Dennison, D and Al Rawas, A H

Aims & Objectives: HSCT is the only curative option for children with sickle cell anemia(SCA). We aim to establish an optimal conditioning regimen with minimal acute and long term toxicity. Patients/Materials & Methods: We performed a retrospective analysis of children who underwent HSCT for SCA, from matched sibling, at a tertiary centre in India (2006-2018). 34 patients received conditioning with Treosulphan (14mg/m2/day X 3 days), Thiotepa (8mg/kg/day X 1 day), Fludarabine (40mg/m2/day X 4 days) with or without low dose ATG. Results: The male female ratio was 1.2:1. Mean age at transplant was 9 years. 85% patients were from Oman and 15%, South Africa. The most common indication for transplant was vaso-occlusive crisis(51%), followed by regular transfusions(23%). The source of stem cells were bone marrow(40%) and peripheral blood(60%). The median time to neutrophil engraftment was 12.2. days and for platelets,17.8days. The day-28 donor chimerism varied from 93% to 100% with a durable graft. Only one patient had stable mixed chimerism necessitating donor lymphocyte infusion. The 100 day mortality was low at 5.8% (acute grade 4 gut GVHD). 5% patients had limited chronic GVHD. Discussion & Conclusion: The Treosulphan based protocol was well tolerated in all age groups and patients exhibited stable chimerism, no intracranial bleed, no SOS, low risk of chronic GVHD and no adverse impact on long term growth, development and possible puberty. Hence this is the most optimal conditioning regimen for patients with sickle cell anemia,.

53. Bone marrow transplantation for sickle cell anemia: is it the right choice?

1997

Indian pediatrics

Gupta, P

54. Efficacy of oral zinc therapy in the management of sickle cell crises

1987

Indian Journal of Medical Research

Gupta, V L and Chaubey, B S

55. Dexmedetomidine as sedative and analgesic in a patient of sickle cell disease for total hip replacement

2013

Indian Journal of Anesthesia

Dhansura, Tasneem and Kapadia, Shakir and Gandhi, Shweta

REVIEWS

1. **Genetic modifiers of sickle cell disease**

   2011

   Hemoglobin

   Thein, S L

Sickle cell disease is one of the best characterized human monogenic disorders. Complex genotype/phenotype correlations clearly demonstrate the interaction of multiple genetic and environmental factors. In the last 20 years, scientific research has applied genetic approaches to dissect some of these modifiers. This review highlights the more recent genetic association studies that have been applied to unravel the genetic modifiers of sickle cell disease including Hb F genetics, and the key genetic variants identified. Illumination of such modifying factors may guide future therapeutic interventions and improve prediction of disease severity, with implications for genetic counseling, prenatal diagnosis and implementation of high risk therapy. Â© 2011 Informa Healthcare USA, Inc.

2. **Polymorphisms associated with the Arab-Indian haplotype of sickle cell anemia are candidate fetal hemoglobin gene modulators**

   2015

   Blood

   Vathipadiekal, V and Alsultan, A and Farrell, J and Al-Rubaish, A M and Al-Muhanna, F and Naserullah, Z and Alsuliman, A and Patra, P K and Milton, J and Farrer, L and Chui, D H K and Al-Ali, A and Sebastiani, P and Steinberg, M H

Fetal hemoglobin (HbF) inhibits HbS polymerization. Because of this, sufficient HbF in most sickle erythrocytes can lead to a milder disease phenotype. HbF levels differ amongst the Î²-globin gene (HBB) cluster haplotypes of sickle cell anemia. In the Arab-Indian (AI) haplotype, HbF was about 20% compared with 5-10% in the Bantu, Benin, and Senegal haplotypes. Functional elements linked to the HBB haplotype are likely to regulate the expression of HbF in addition to the effects of trans-acting modulators. To identify cis-acting SNPs in the HBB gene cluster that differentiate the AI haplotype from all others, including the Senegal haplotype-the Senegal haplotype shares some SNPs with the AI haplotype but its carriers have lower HbF-we studied patients with sickle cell anemia who were homozygous for HBB haplotypes by genome-wide SNP association analysis (GWAS; Table). First, we compared the results of GWAS of 42 Saudi AI haplotype homozygotes with GWAS in 71 Saudi Benin haplotype homozygotes. The only variants distinguishing these 2 populations with genome-wide significance (p-values between 9.6E-07 and 2.7E-45) were 223 SNPs in chromosome 11p15 from positions 3.5 to 6.5 mb. This region included the HBB gene cluster, its locus control region (LCR) and the upstream and downstream olfactory receptor gene clusters. The minor allele frequency of SNPs in MYB (chr 6q23), BCL11A (chr 2p16) and KLF1 (chr 19), trans-acting loci that affect expression of the HbF genes, were similar in these 2 cohorts. A novel candidate trans-acting locus was not found, however our power to detect such an association was low. We followed-up these observations by comparing allele frequencies in 303 African American cases homozygous for the haplotypes shown in the Table. Thirteen GWAS-significant SNPs, in addition to rs7482144 and rs10128556, were present in all AI haplotype cases but not in 83 Senegal haplotype chromosomes. The allele frequency of these SNPs was replicated in 62 independent AI haplotype cases. Rs2472530 is in the coding region of OR52A5; rs16912979, rs4910743 and rs4601817 are in the HBB gene cluster LCR; rs16912979 in DNase I hypersensitive site-4 altered motifs for POLR2A, GATA1, and GATA2 binding.The minor allele of rs10837771 causes a missense mutation in OR51B4 an upstream olfactory receptor gene. To see if any of these or other alleles might sometimes be associated with HbF in the Bantu and Benin haplotyes, we selected homozygotes and

compound heterozygous for these haplotypes who had unexplained and uncharacteristically high HbF. Thirty-one African Americans, aged â‰¥5 yrs. who had a HbF of 21% were compared with 350 similar cases who had a mean HbF of 3%. Four additional SNPs on chromosome 11, from positions ranging from 5536415 to 5543705 in the UBQLNL/HBG2, region and present in 45-48% of AI haplotype and 3-13% of other haplotypes, were found at higher frequencies in the high HbF group compared with the low HbF group. These SNPs also altered transcription factor binding motifs. Loci marked by SNPs that distinguish the AI from the Senegal and other HBB haplotypes might contain functionally important polymorphisms and account in part for high HbF in AI haplotype sickle cell anemia, independent of, or in addition to, the effects associated with rs7482144 or rs10128556. They might also be rarely associated with high HbF found in other haplotypes. These observations provide a foundation for mechanistic studies focused on the role of these variants in the expression of their linked HbF genes. (Table Presented).

3. **The influence of HBF on the pathophysiology and phenotype of sickle cell disease**

   2016

   Vox Sanguinis

   Adekile, A D

HbS results from the substitution of valine for glutamic acid in the 6th amino position in the b-globin chain. Its inheritance as a homozygote or compound heterozygote causes sickle cell disease (SCD). The central paradigm in the pathophysiology of the disease is the reduced solubility of HbS in a deoxygenated medium, which causes rigidity and distortion of the red blood cell (RBC) membrane with increased viscosity and other rheological abnormalities. There is a chronic hemolytic anemia and occlusion of small blood vessels, which is responsible for the characteristic recurrent pain episodes of SCD. It is, however now recognized that SCD is a chronic inflammatory disease because of extensive vasculopathy, instigated by the free heme from hemolysis, which sets off a cascade of pro-inflammatory signaling mechanisms with upregulation of adhesion molecules, platelet activation, thrombin generation and ischemia/reperfusion injury. Nitric oxide depletion results in vasoconstriction, and eventual endothelial intima proliferation. This endothelial dysfunction drives SCD subphenotypes like stroke, pulmonary hypertension, priapism and chronic leg ulcers. On the other end of the spectrum, the viscosity-driven subphenotypes include recurrent pain episodes, acute chest syndrome and osteonecrosis. Several genetic factors including single-gene polymorphisms within the Î²-globin gene cluster and in distant loci, act as SCD phenotype modifiers. The most recognized of these is HbF and patients with levels of â‰¥20% have a mild phenotype. Kuwaiti SCD patients have HÎ²F levels >30% in the first 3 years of life and 15-20% in older patients. They carry the Arab/India Î²S-globin haplotype and there is a high prevalence of Î±-thalassemia trait, which also modulates the phenotype. The patients generally have a mild phenotype in childhood; stroke, priapism and chronic leg ulcers are rare. In addition, silent brain infarcts are uncommon in children and their neurocognitive function is comparable to that in their normal siblings. However, osteonecrosis is common with a prevalence of about 25% in children and >45% in adults. The only predisposing factor is frequent pain episodes; sex, co-existent athal trait or bone morphogenic protein polymorphisms have not shown any association with osteonecrosis in these patients. In spite of elevated HbF levels, Kuwaiti patients with HbSD or HbSÎ²thal tend to have a severe phenotype. In the former, it's probably because of the pro-sickling nature of the b121Glu>Gln substitution of HbD, while in the latter it may be due to the nature of the Î²-thal mutation. Even Kuwaiti patients with HbSb+-thal do have frequent severe pain crises. Elevated HbF level is therefore not uniformly protective and the SCD phenotype in adult Kuwaiti SCD patients is, quite often, quite severe. More studies are clearly indicated in this group of patients.

4. **Review of therapeutic apheresis procedures in a tertiary care hospital in india**

   2012

   Vox Sanguinis

   Deshpande, A and Kalgutkar, S and Kulkarni, M

Background: Therapeutic apheresis has a role in various acute and chronic disease conditions. Therapeutic plasma exchange is life saving in acute neurological conditions like myasthenia gravis (MG) crisis or Guillain Barre syndrome (GBS) and particularly hemolytic uremic syndrome (HUS) in children. In patients with severe malaria, babesiosis, sickle cell disease, therapeutic red cell exchange is beneficial. Aims: To review therapeutic plasma exchange (TPE) and red cell exchange (TREX) procedures. To compare use of continuous flow and intermittent flow cell separators in TPE. Methods: A retrospective analysis of 422 TPE, 05 TREX procedures carried out during last 13 years at our hospital was done. Total 92 procedures were carried out using intermittent flow cell separator and continuous flow cell separator was used in 330 procedures of TPE. For TREX continuous flow cell separator was used. Results: Total 422 TPE procedures in 74 patients (17 - pediatric, 57 - adult) were carried out. Myasthenia gravis (54%) was the commonest indication followed by GBS and HUS. On an average five procedures per patient were required for neurological disorders but number of procedures required for other disorders was more. On an average 1.5 volume plasma was exchanged with FFP or colloids and crystalloids as replacement fluids. The time required for the procedure using intermittent flow cell separator ranged from 130 to 200 min as compared to 33-130 min with continuous flow cell separator. Citrate toxicity (n = 7) was the commonest complication, others were low access pressure (n = 2), reversible hypotension (n = 2) and allergic reactions to FFP transfusions (n = 1). Clinical outcome was satisfactory in neurological disorders as well as HUS cases in children. Total 05 TREX procedures were carried out in two pediatric patients with malaria and one adult patient with sickle cell disease. The time required for TREX in pediatric patients was 90 min and in adult patient ranged from 97 to 117 min. Group specific cross-matched packed red blood cells were used as replacement fluid. In cases of malaria the infestation rate dropped from 75% to 18% and 67% to 08% after the procedure. In the patient with sickle cell disease, Hb S levels dropped to <20% after every single procedure. All the five procedures were uneventful. Conclusions: Therapeutic apheresis procedures (TPE, TREX) are safe and effective in various clinical disorders. Continuous flow cell separators are more effective and require less time for the procedure as compared with intermittent flow cell separators.

5. **Management of sickle cell disease in patients undergoing cardiac surgery**

   2017

   Journal of Cardiac Surgery

   ***Crawford, T C and Carter, M V and Patel, R K and Suarez-Pierre, A and Lin, S Z and Magruder, J T and Grimm, J C and Cameron, D E and Baumgartner, W A and Mandal,* K**

Sickle cell disease is a life-limiting inherited hemoglobinopathy that poses inherent risk for surgical complications following cardiac operations. In this review, we discuss preoperative considerations, intraoperative decision-making, and postoperative strategies to optimize the care of a patient with sickle cell disease undergoing cardiac surgery.

6. **A review on phytochemical and pharmacological reserch - Remedy for sickle cell disease**

   2016

   International Journal of Pharmaceutical Sciences and Research

   Vaishnava, S and Rangari, V D

This article focuses on the current review of world-wide medicinal plants studied for their phytochemical investigations, various biological activities and clinical studies in relation to their use for treatment of Sickle cell disease. Method: All relevant literature databases were searched up to 18 September 2014. The search terms were plant, herb, herbal therapy, phytotherapy, sickle cell anemia and antisickling agent. All of the human, animal, in vitro studies, and reviews were included. Antisickling agent, antioxidant, and ethnopharmacological effects were the key outcomes. Results: In vitro and in vivo studies in various herbs revealed that anthraquinones, anthocaynin, amino acids, caricapinoside, p-hydroxy benzoic acid etc. are the potent herbal constituents responsible for antisickling activity in sickle cell anemia patients and these herbal constituents can be further researched for development of a much safer and affordable medicine in future. Conclusion: This extensive literature review

indicated the presence of large number of medicinal plants and their phytochemical constituents that can be of great interest for further research in search of the therapeutically active natural products for the treatment of sickle cell disease. However, it implies from the present review that comparatively very less number of medicinal plants have been explored in search of the constituents for the antisickling activity. Extensive medicinal plant research in the area of sickle cell disease may open completely new vistas and treatment strategies for this incurable genetic disorder.

7. **Peripheral blood smear analysis using image processing approach for diagnostic purposes: A review**

   2018

   Biocybernetics and Biomedical Engineering

   Hegde, R B and Prasad, K and Hebbar, H and Sandhya, I

Peripheral blood smear analysis is a common practice to evaluate health status of a person. Many disorders such as malaria, anemia, leukemia, thrombocytopenia, sickle cell anemia etc., can be diagnosed by evaluating blood cells. Many groups have reported methods to automate blood smear analysis for detection of specific disorders for diagnostic purposes. In this paper, we have summarized the methods used to analyze peripheral blood smears using image processing techniques. We have categorized these methods into three groups based on approaches such as WBC analysis, RBC analysis and platelet analysis. We conclude that there is a need for a method of automation to match with human evaluation process and rule out any abnormality present in the blood smear. It is desirable for studies on automation of peripheral blood smear analysis to focus on development of robust method to handle illumination and color shade variations. Also, it is desirable to design a method which could collect all the abnormal regions from all views of a specimen to limit the manual evaluation to those regions making it more feasible for telemedicine applications.

8. **PRO6 comparative efficacy and safety of crizanlizumab for adults with sickle-cell disease: a network meta-analysis**

   2019

   Value in Health

   Thom, H Z and Jansen, J P and Shafrin, J and Zhao, L and Joseph, G J and Cheng, H Y and Gupta, S and Shah, N

Objectives: To compare the efficacy and safety of crizanlizumab (5mg/kg) with other treatments for sickle cell disease (SCD) among young adult and adult (â‰¥16 years old) SCD patients not well managed by hydroxyurea via network meta-analysis. Methods: A systematic literature review of MEDLINE, Embase, CENTRAL, and clinical trials registries for studies on treatment efficacy in young adult and adult SCD patients identified 65 relevant full-text publications evaluating 49 studies. Networks of randomized controlled trial (RCT) evidence on treatments connected to crizanlizumab 5mg/kg identified for pain crisis, hospitalization, adverse events (AE), and serious adverse events (SAE). Hydroxyurea was not included as the study population was patients that were ineligible, failed or failing on hydroxyurea; transfusions were not included as only study identified was not placebo-controlled. The analysis combined treatment effects relative to placebo estimated by RCTs, thus balancing prognostic factors. Bayesian shared parameter model, using vague priors, combining relative treatment effects was used to analyze all studies simultaneously. Results: The pain crisis network consisted of 5 RCTs on 10 treatments, hospitalization days network consisted of 4 RCTs on 6 treatments, AE network consisted of 5 RCTs on 7 treatments, and SAE network of 5 RCTs on 8 treatments. Crizanlizumab was more efficacious than L-glutamine on pain crisis prevention (HR= 0.67, 95% credible interval (CrI)=0.50-0.88, Bayesian one-sided p-value 0.002). There was no or limited evidence of a difference between crizanlizumab and L-glutamine on hospitalization day, AE, or SAE rates based on Bayesian one-sided p-values. Results on other treatments (one or multiple doses each of N-acetylcysteine, prasugrel, senicapoc, ticagrelor, and transfusions) were too weak to draw conclusions. Conclusions: Crizanlizumab 5mg/kg is more efficacious than L-glutamine in preventing pain crises

in adults. There was limited evidence of a difference on AE, SAE, and hospitalization day rates across treatments. Results versus other treatments were inconclusive.

9. **An overview on sickle cell disease profile**

   2013

   Asian Journal of Pharmaceutical and Clinical Research

   Kaur, M and Dangi, C B S and Singh, M

Sickle cell disease (SCD) is a very devastating condition caused by an autosomal recessive inherited haemoglobinopathy. This disease affects millions of peoples globally which results in serious complications due to vasoocclusive phenomenon and haemolysis. This genetic abnormality is due to substitution of amino acid valine for the glutamic acid at the sixth position of beta chain of haemoglobin. This disease was described about one hundred year ago. The haemoglobin S (hbS) produced as result of this defect is poorly soluble and polymerized when deoxygenated. Symptoms of sickle cell disease are due to chronic anaemia, pain full crises, acute chest syndrome, stroke and susceptibility to bacterial infection. In recent years measures like prenatal screening, better medical care, parent education, immunization and penicillin prophylaxis have successfully reduced morbidity and mortality and have increased tremendously life expectancy of affected individuals. Three principal current therapeutics modalities available for childhood SCD are blood transfusion, Hydroxy urea and bone marrow transplantation. Genetic counseling, continued medical education for health professionals about sickle cell disease, its complications and management is necessary. World health organization has actively promoted several national screening programms with dual goals of informing reproductive choice and thereby reducing the number of severely affected children.

10. **Clustered regularly interspaced short palindromic repeat technique in correcting sickle cell anemia - A review**

    2018

    Drug Invention Today

    Rajpurohit, G K and Gayathri, R and Vishnu Priya, V

The human hemoglobin is made up of two alpha and two beta chains. In sickle cell anemia, the sixth position of the beta chain is affected, and glutamic acid is substituted for valine. Clustered regularly interspaced short palindromic repeat (CRISPR) can be used to edit the beta chain. This technique can be used to cut the DNA sequence at the desired location and thus is a very precise technique to correct the genetic disease.

11. **A meta-analysis of endothelial nitric oxide synthase gene T786C polymorphism as a risk factor for acute chest syndrome in sickle cell disease**

    2021

    Meta Gene

    Kumar, R and Mishra, S and Shrivastava, S

Objective: The aim of this meta-analysis was to determine association of the endothelial nitric oxide synthase (eNOS) T786C polymorphism with the susceptibility of acute chest syndrome in sickle cell disease patients. Methods: Meta-analysis was conducted by pooling the results of 5 eligible studies that were retrieved from Pubmed, Pubmed Central, Science Direct and Google Scholar. Results: After carrying out the meta-analysis of pooled samples, no significant association of eNOS T786C polymorphism with acute chest syndrome in sickle cell disease patients was identified. There was moderate to high degree of heterogeneity in the data in all the genotypic and allelic models. There was no publication bias as evident from Egger's test. No subgroup analysis

was made due to lack of sufficient data. Conclusion: The present study deliberates the T786C eNOS gene polymorphism is not a significant risk factor for the acute chest syndrome in sickle cell disease patients.

12. **Multi-institutional, retrospective review of blood transfusion practices and outcomes in a large cohort of thalassemia patients in South India**

    2017

    Pediatric Hematology Oncology Journal

    Agarwal, R K and Sedai, A and Ankita, K and Parmar, L and Dhanya, R and Dhimal, S and Shriniwas, R and Sumithra, P and Iyer, H V and Gowda, A and Gujjal, P and Pradeep, R and Pushpa, H and Jain, S and Kondaveeti, S and Dasaratha Ramaiah, J and Raviteja and Sharma, H and Jali, S and Viragi, S and Bobati, S and Tallur, N R and Ramprakash, S and Faulkner, L

13. **Susceptibility to vascular complications in sickle cell anemia patients is associated with intron 4a/b polymorphism of the NOS3 gene: A meta-analysis**

    2021

    Meta Gene

    Bhaskar, L.V.K.S.

Background: Sickle cell anemia (SCA) is characterized by chronic hemolysis and vaso-occlusive episodes. The endothelial dysfunction in SCA may be due to the deficiency of nitric oxide. The association between nitric oxide synthase (NOS3) gene polymorphisms (â’’786 T > C, 894G > T and intron 4a/b) and risk of vascular complications remains elusive. Objective: Here we performed a meta-analysis to evaluate the relationship between NOS3 gene polymorphisms and vascular complications of SCA. Methods: Ten previously published articles were retrieved from PubMed, and Embase bibliographic databases. This meta-analysis included, eight papers (463 SCA patients with complications and 333 without complications) that pertained to the NOS3 -786 T > C, five papers (235 SCA patients with complications and 191 without complications) that corresponded to the NOS3 894G > T polymorphism and six papers (391 SCA patients with complications and 292 without complications) that involved the NOS3 intron 4a/b polymorphism. Pooled analysis, sensitivity analysis and assessment of publication bias were performed. Results: Results of pooled analysis revealed that the NOS3 intron 4a/b polymorphism was significantly associated with an increased risk of vascular complications (aa+ab Vs. bb: odds ratio = 3.28, 95% confidence interval = 1.19â€“9.02, p = 0.022, random-effect model). However, no significant association was found for NOS3 -786 T > C and 894G > T polymorphisms. Conclusion: Despite some limitations, our meta-analysis suggests that NOS3 intron 4a/b polymorphism is associated with four fold-increased risk of vascular complications in sickle cell anemia.

14. **Pain Management Issues as Part of the Comprehensive Care of Patients with Sickle Cell Disease**

    2018

    Pain management nursing : official journal of the American Society of Pain Management Nurses

    Lakkakula, B.V.K.S. and Sahoo, R and Verma, H and Lakkakula, S

BACKGROUND: Vaso-occlusive pain crisis is one of the primary complications of sickle cell disease (SCD) and is responsible for the majority of hospital visits in patients with SCD. Stints of severe pain can last for hours to days and are difficult to treat and manage, often resulting in drastically reduced quality of life. PURPOSE: Our purpose is to provide an overview of pain management issues in SCD populations. METHODS: We explored literature using PubMed and Embase for the etiology and management of pain in SCD. Databases were searched employing the following terms: sickle cell, pain pathways, pain perception, pharmacological therapies, psychological therapies, physical therapies and genetics. RESULTS: Pain in SCD can vary from acute to chronic (persistent) or mixed and understanding of the underlying mechanisms is important for proper pain management.

Currently, there are many means of managing pain in children with SCD, which involve pharmacological and non-pharmacological approaches. A combination of psychotherapy and pain medications can be used for treatment of pain and other psychosocial co-morbidities in complex persistent pain. CONCLUSIONS: Providing more appropriate medication and optimal dosage based on individual's genomic variations is the future of medicine, and this will allow the physicians to hone in on optimal pain management in patients with SCD.

15. **Review of therapeutic apheresis procedures in a tertiary care hospital in India**

    2013

    Indian Journal of Hematology and Blood Transfusion

    Kalgutkar, S and Sawant, R and Deshpande, A

Introduction: Therapeutic apheresis has a role in various acute & chronic disease conditions. Therapeutic plasma exchange is beneficial in myasthenia gravis (MG) crisis or Guillain Barre syndrome (GBS) and hemolytic uremic syndrome (HUS) in children. In patients with severe malaria, sickle cell disease, therapeutic red cell exchange is beneficial. Aims: To review therapeutic plasma exchange (TPE) & red cell exchange (TREX) procedures. To compare use of continuous flow (CFCS) & intermittent flow cell separators (IFCS) in TPE. Materials and Methods: A retrospective analysis of 438 TPE, 07 TREX procedures carried out in both adult and pediatric patients during a 13 year period was done. 92 procedures were carried out using IFCS & CFCS was used in 346 procedures for TPE. For TREX CFCS was used. Results: 438 TPE procedures in 77 patients (18- pediatric, 59-adult). Myasthenia gravis, GBS & HUS were the commonest indications. An average of 5 procedures per patient were required for clinical benefit. 1.5 volume plasma was exchanged with FFP or colloids & crystalloids as replacement fluids. Procedure time with IFCS was from 130-200 and 33-130 min with CFCS. Citrate toxicity,low access pressure, reversible hypotension and allergic reactions was the commonest complications. Clinical outcome was satisfactory. 07 TREX procedures, in 2 pediatric patients with malaria, 2 with sickle cell disease (SCD) & one adult patient with SCD. The procedure time ranged from 52-90 and 97-117 min in adult patient. Group specific cross-match compatible packed red blood cells were used as replacement fluid. In cases of malaria the infestation rate dropped from 75-18 and 67-08 % after the TREX. In the adult patient with SCD, Hb S levels dropped to<20 % after each procedure and in pediatric patients HbS levels dropped five fold in both cases post procedure. Conclusion: Therapeutic apheresis procedures (TPE, TREX) are safe & effective in various clinical disorders. CFCS are well tolerated by patient and require less procedure time. Therapeutic apheresis can be safely performed in patients of pediatric age group maintaining their hemodynamic stability.

16. **The evolution of clinical research in thalassaemia: where has all the funding gone?**

    2020

    British Journal of Haematology

    Rund, D

17. **A study of chronic red cell transfusions in thalassemia and sickle cell disease patients with emphasis on auto/alloimmunization and selection of blood units, review of 230 transfusion episodes in 33 patients**

    2014

    Indian Journal of Hematology and Blood Transfusion

    VijayaLaxmi, S and Shanthi, B and Vishala Sharma, C and Jain, S

Background: Transfusions are the primary therapy for thalassemia and sickle cell disease but have significant complications and expose the patients to a variety of risks. Continuous blood transfusion can causes alloimmunization against RBC antigens and complicate further treatment in these patients, Alloimmunization to

red cell antigens is one of the most important immunological transfusion reaction and results in ineffective transfusion. However, few data are available on the frequency of RBC alloimmunisation in the Indian population with history of chronic transfusions. Extended phenotype matched blood may help in decreasing the rate of alloimmunization and effectiveness of transfusion. Aim of the Study: The purpose of this study is to evaluate the frequency of RBC allo and auto antibodies and the role of extended Rh and Kell phenotype matched blood to prevent alloimmunization. Materials and Methods: Reviewed all the red cell transfusions given to clinically diagnosed patients of thalassemia major, intermedia and sickle cell anemia/disease patients between Aug 2011 and Aug 2014 Total 33 patients and 230 blood transfusion work up were reviewed. ABO Rh and Kell grouping was done, direct and indirect Coomb's test, Antibody screening for auto and allo antibodies, Anti body identification and Coomb's cross match were performed by column agglutination method. Results: Allo antibodies like anti-c, E, e, C, D(Rh system), Kell, Xga, Duffy were identified in the patients. 9 patients presented with both auto and allo antibodies. Rh extended and Kell along with ABO typing done for the donors for each transfusion. Conclusion: Rh and Kell extended phenotype matched blood helped in preventing delayed haemolytic reactions. RBC allo antibodies in our patients with Î²-thalassemia were mostly Rh system antibodies. The development of RBC allo and auto antibodies was associated with previous transfusion reactions. Rh and Kell extended Phenotyping also helped in preventing further alloimmunization.

18. **Five Rare [beta] Globin Chain Hemoglobin Variants in India**

    2016

    Indian Journal of Hematology and Blood Transfusion

    Colah, Roshan B and Nadkarni, Anita and Gorakshakar, Ajit and Sawant, Pratibha and Gorivale, Manju and Mehta, Pallavi and Sawant, Madhavi and Ghosh, Kanjaksha

Thalassemias as well as structural hemoglobin (Hb) variants are common monogenic inherited disorders of Hb in India. In this paper we describe 5 rare [beta]-chain Hb variants identified in the Indian population on the basis of high performance liquid chromatography (HPLC). Of these 3 were identified during antenatal screening of [beta]-thalassemia while the other 2 cases were referred to us for a diagnostic work up. These 5 Hb variants were Hb British Columbia ([beta] CD 101 GAG [arrow right] AAG), Hb Saint Louis ([beta] CD28 CTG [arrow right] CAG), Hb G Coushatta ([beta] CD 22 GAA [arrow right] GCA), Hb Pyrgos ([beta] CD 83 GGC [arrow right] GAC) and Hb Agenogi ([beta] CD 90 GAG [arrow right] AAG). Hb Saint Louis and Hb G Coushatta eluted in the HbA2 window, Hb British Columbia and Hb Agenogi eluted in the Hb C window while Hb Pyrgos eluted in an unknown window on HPLC. They were all identified by DNA sequencing. The child having Hb St. Louis had hepatosplenomegaly and anemia while the individuals with the other 4 variants were asymptomatic. Rare Hb variants are diagnostic curiosities that may be encountered by laboratories. Correct identification requires the application of more than one technique to avoid misdiagnosing them as more common variants (e.g. St. Louis and G Coushatta as E or D Iran on HPLC. Some, like G Coushatta may interfere with HPLC-based HbA1c estimation).

19. **Crizanlizumab and comparators for adults with sickle cell disease: a systematic review and network meta-analysis**

    2020

    BMJ Open

    Thom, Howard and Jansen, Jeroen and Shafrin, Jason and Zhao, Lauren and George, Joseph and Hung-Yuan, Cheng and Gupta, Subhajit and Shah, Nirmish

Objectives Treatment options for preventing vaso-occlusive crises (VOC) among patients with sickle cell disease (SCD) are limited, especially if hydroxyurea treatment has failed or is contraindicated. A systematic literature review (SLR) and network meta-analysis (NMA) were conducted to evaluate the efficacy and safety of crizanlizumab for older adolescent and adult (â‰¥16 years old) SCD patients.MethodsThe SLR included randomised controlled trials (RCTs) and uncontrolled studies. Bayesian NMA of VOC, all-cause hospitalisation

days and adverse events were conducted.ResultsThe SLR identified 51 studies and 9 RCTs on 14 treatments that met the NMA inclusion criteria. The NMA found that crizanlizumab 5.0 mg/kg was associated with a reduction in VOC (HR 0.55, 95% credible interval (0.43, 0.69); Bayesian probability of superiority >0.99), all-cause hospitalisation days (0.58 (0.50, 0.68); >0.99) and no evidence of difference on adverse events (0.91 (0.59, 1.43) 0.66) or serious adverse events (0.93 (0.47, 1.87); 0.59) compared with placebo. The HR for reduction in VOC for crizanlizumab relative to L-glutamine was (0.67 (0.50, 0.88); >0.99). These results were sensitive to assumptions regarding whether patient age is an effect modifier.ConclusionsThis NMA provides preliminary evidence comparing the efficacy of crizanlizumab with other treatments for VOC prevention.

20. **Medical disease as a cause of maternal mortality:the pre-imminence of cardiovascular pathology**

    2016

    Cardiovascular Journal of Africa

    Mocumbi, A O and Sliwa, Karen and Soma-Pillay, P

Abstract Maternal mortality ratio in low- to middle-income countries (LMIC) is 14 times higher than in high-income countries. This is partially due to lack of antenatal care, unmet needs for family planning and education, as well as low rates of birth managed by skilled attendants. While direct causes of maternal death such as complications of hypertension, obstetric haemorrhage and sepsis remain the largest cause of maternal death in LMICs, cardiovascular disease emerges as an important contributor to maternal mortality in both developing countries and the developed world, hampering the achievement of the millennium development goal 5, which aimed at reducing by three-quarters the maternal mortality ratio until the end of 2015. Systematic search for cardiac disease is usually not performed during pregnancy in LMICs despite hypertensive disease, rheumatic heart disease and cardiomyopathies being recognised as major health problems in these settings. New concern has been rising due to both the HIV/AIDS epidemic and the introduction of highly active antiretroviral therapy. Undetected or untreated congenital heart defects, undiagnosed pulmonary hypertension, uncontrolled heart failure and complications of sickle cell disease may also be important challenges. This article discusses issues related to the role of cardiovascular disease in determining a substantial portion of maternal morbidity and mortality. It also presents an algorhitm to be used for suspected and previously known cardiac disease in pregnancy in the context of LIMCs.

21. **Evidence review of hydroxyurea for the prevention of sickle cell complications in low-income countries**

    2013

    Archives of Disease in Childhood

    Mulaku, Mercy and Opiyo, Newton and Karumbi, Jamlick and Kitonyi, Grace and Thoithi, Grace and English, Mike

Hydroxyurea is widely used in high-income countries for the management of sickle cell disease (SCD) in children. In Kenyan clinical guidelines, hydroxyurea is only recommended for adults with SCD. Yet many deaths from SCD occur in early childhood, deaths that might be prevented by an effective, disease modifying intervention. The aim of this review was to summarise the available evidence on the efficacy, effectiveness and safety of hydroxyurea in the management of SCD in children below 5 years of age to support guideline development in Kenya. We undertook a systematic review and used the Grading of Recommendations Assessment, Development and Evaluation system to appraise the quality of identified evidence. Overall, available evidence from 1 systematic review (n=26 studies), 2 randomised controlled trials (n=354 children), 14 observational studies and 2 National Institute of Health reports suggest that hydroxyurea may be associated with improved fetal haemoglobin levels, reduced rates of hospitalisation, reduced episodes of acute chest syndrome and decreased frequency of pain events in children with SCD. However, it is associated with adverse events (eg, neutropenia) when high to maximum tolerated doses are used. Evidence is lacking on whether hydroxyurea improves survival if given to young

children. Majority of the included studies were of low quality and mainly from high-income countries. Overall, available limited evidence suggests that hydroxyurea may improve morbidity and haematological outcomes in SCD in children aged below 5 years and appears safe in settings able to provide consistent haematological monitoring.

22. **Hydroxyurea in Sickle Cell Disease: Drug Review**

    2014

    Indian Journal of Hematology and Blood Transfusion

    Agrawal, Rohit Kumar and Patel, Rakesh Kantilal and Shah, Varsha and Nainiwal, Lalit and Trivedi, Bhadra

Hydroxyurea, a myelosuppressive agent, is the only effective drug proven to reduce the frequency of painful episodes. It raises the level of HbF and the haemoglobin level. It usually decreases the rate of painful episodes by 50 %. It was first tested in sickle cell disease in 1984. It also decreases the rate of ACS episodes and blood transfusions by ~50 % in adults. It was developed as an anticancer drug and has been used to treat myeloproliferative syndromes-leukemia, melanoma, and ovarian cancer. It was approved for use by FDA in adults. Side effects includes neutropenia, bone marrow suppression, elevation of hepatic enzymes, anorexia, nausea, vomiting and infertility.

23. **A Systematic Review of Pharmacological Therapies for Sickle Cell Disease**

    2011

    Biomedical & Pharmacology Journal

    Nikhar, H S and Meshram, S U and Shinde, G B

This review was carried out to understand various issues concerned with the patients of sickle cell disease (SCD). An attempt has been made to review the literature with respect to the multiple complications experienced by the SCD patients, variety of pharmacological therapies used throughout the world for SCD management. The literature highlighted the lack of reliable prevalence statistics, lower use of diagnostic measures, especially in rural areas. The literature indicated that varieties of medicinal plants are used regularly for the management of SCD related complications, such as sickling, infections, pain crisis, etc. Although, Bone marrow transplant, the only curative therapy and genetic counselling, have shown promising results for effective management of SCD, now a days people are using alternative pharmacological therapies for SCD management

24. **Ethical issues in genetic counselling with special reference to haemoglobinopathies**

    2011

    The Indian Journal of Medical Research

    Muthuswamy, Vasantha

Genetic counselling is provided in places where genetic tests are carried out. The process involves pre-test counselling as well as post-test counselling to enable the individuals to face the situation and take appropriate decisions with the right frame of mind. Major ethical principles which govern the attitudes and actions of counsellors include: respect for patient autonomy, non-maleficence, beneficence, or taking action to help benefit others and prevent harm, both physical and mental, and justice, which requires that services be distributed fairly to those in need. Other moral issues include veracity, the duty to disclose information or to be truthful, and respect for patient confidentiality. Nondirective counselling, a hallmark of this profession, is in accordance with the

principle of individual autonomy. High prevalence of haemoglobinopathies with availability of good and sensitive carrier detection tests and prenatal diagnostic techniques makes these good candidates for population screening of carriers along with genetic counselling for primary prevention of the disease. Screening of the extended family members of the affected child, high risk communities and general population screening including antenatal women are the main target groups for planning a Haemoglobinopathy control programme. A critical mass of trained genetic counsellors who have understanding of the ethical issues and its appropriate handling with the required sensitivity is needed in India.

25. **How to setup a successful transplant program for hemoglobinopathies in developing countries: The Cure2Children approach.**

    2020

    Hematology/oncology and stem cell therapy

    Faulkner, Lawrence

Hematopoietic stem cell transplantation (HSCT) remains the only established definitive cure for severe hemoglobinopathies, such as sickle cell disease (SCD) and thalassemia-the most prevalent life-threatening non-communicable disease of childhood globally. HSCT can not only cure over 85% of children with a compatible sibling but also restore normal health-related quality of life in most cases who do not have major irreversible organ damage at transplant. In low- and middle-income countries (LMICs), particularly in sub-Saharan Africa, SCD carrier rate can be up to 30% and 1% of live births have SCD. Relatively simple and inexpensive measures such as newborn screening, early diagnosis, caregiver education, and timely institution of anti-pneumococcal prophylaxis and hydroxyurea therapy can substantially reduce SCD-related mortality and morbidity. Improved prevention and early care should proceed in parallel with the development of transplant services and hope for cure. Cure2Children, an Italian NGO, has supported the startup of several bone marrow transplantation programs in LMICs where over 500 transplants have been performed over the last 10Â years, with outcomes not substantially different from high-income countries but at a fraction of the cost. This report summarizes this experience and suggests some strategies to set up new HSCT units.

26. **Phytomedicines (medicines derived from plants) for sickle cell disease.**

    2004

    The Cochrane database of systematic reviews

    Cordeiro, N J V and Oniyangi, O

BACKGROUND: Sickle cell disease (SCD) is a common recessively inherited disorder of haemoglobin affecting peoples originating from sub-Saharan Africa, the Middle East and Mediterranean basin, the Indian subcontinent, the Caribbean and South America. The homozygous state (SS) is associated with complications and a reduced life expectancy. Phytomedicines (medicine derived from plants in their original state) encompass much of what the populations most affected would encounter in terms of plant-remedies from traditional healers. There has been little in the way of systematic appraisal of their benefits. OBJECTIVES: To assess the benefits and risks of phytomedicines in people with SCD of all types, of any age, in any setting. SEARCH STRATEGY: We searched the Cochrane Cystic Fibrosis and Genetic Disorders group specialised register of controlled trials of haemoglobinopathies, which comprises references identified from comprehensive electronic database searches, handsearches of relevant journals and abstract books of conference proceedings. We performed an additional search of the bibliographic database of Allied and Complementary Medicine (AMED). Date of most recent search of the trials register: September 2003. SELECTION CRITERIA: All randomised or quasi-randomised trials with participants of all ages with SCD, in all settings, comparing the administration of phytomedicines, by any mode to placebo or standard treatment, including blood transfusion and hydroxyurea. DATA COLLECTION AND

ANALYSIS: Both reviewers independently assessed trial quality and extracted data from the study. MAIN RESULTS: Reports of two trials were found, of which only one, including 82 participants, was eligible for inclusion in this review. This Phase IIB (pivotal) study suggests that a phytomedicine, NIPRISAN, was effective in reducing episodes of SCD crisis associated with severe pain over a six-month period. NIPRISAN did not appear to affect the risk of severe complications or the level of anaemia. No serious adverse effects were reported. REVIEWERS' CONCLUSIONS: While NIPRISAN, as a phytomedicine, appeared to be safe and effective, over a six-month follow-up period of this study, in reducing crises associated with severe pain, further studies are required to assess its role in the management of people with sickle cell disease. The results of Phase III, multicentre trials are awaited.

27. **Sickle cell disease in India: a scoping review from a health systems perspective to identify an agenda for research and action.**

    2021

    BMJ global health

    Raman, Vineet and Seshadri, Tanya and Joice, Sangeetha V and N Srinivas, Prashanth

INTRODUCTION: Sickle cell disease (SCD) disproportionately impacts Adivasi (tribal) communities in India. Current research has focused on epidemiological and biomedical aspects but there has been scarce research on social determinants and health systems aspects. Given its fragmented distribution, resources and programmes have emerged in west and central India. This scoping review seeks to identify geographical and evidence gaps for action on SCD from a health systems lens. METHODS: We followed a scoping review protocol, using Google Scholar and PubMed for published literature. Keywords used included sickle cell anaemia/disease, health systems, tribal and India. We used Google search for grey literature. We compiled a list of 55 records (of which 35 were retained), with about half pertaining directly to India and others relevant to similar settings. Results were organised and analysed using the WHO health systems framework to identify geographical and evidence gaps. RESULTS: We found substantial literature on biomedical and clinical aspects of SCD but little on the design and implementation of programmes in community and Adivasi-specific contexts as well as on social determinants of SCD. There were regional gaps in knowledge in southern and northeast India. Wherever community-based programmes exist, they have originated in civil society initiatives and relatively limited state-led primary healthcare-based efforts pointing to weak agenda setting. CONCLUSION: Both research and action on SCD especially among tribal populations need immediate attention. While geospatial epidemiology has been well understood, gaps remain in context-specific knowledge for action in several parts, as well as evidence gaps across several health system building blocks, including governance and financing of care. Despite publication of a draft policy, delayed adoption and lapses in implementation have limited the response largely to local communities and non-governmental organisations.

28. **Sickle cell anemia/sickle cell disease and pregnancy outcomes among ethnic tribes in India: an integrative mini-review**

    2021

    Journal of Maternal-Fetal and Neonatal Medicine

    Ganesh, B and Rajakumar, T and Acharya, S K and Kaur, H

Objective: To evaluate the studies which have reported the prevalence of maternal complications and outcomes for women with SCA/SCD. Healthy populations make a healthy community and improve the future for mankind. Pregnant women are an essential segment of humanity as they bear the fetus and supply nutrition for their development throughout the gestational period. Their health status and disease conditions also play a vital role in deciding the future of the offspring. Materials and methods: The Mesh terms: â€œHaemoglobinopathiesâ€ + â€œSickle cell anemiaâ€ + â€œSickle cell diseaseâ€ + â€œEthnic tribesâ€ + â€œPregnancy outcomesâ€ + â€œIndiaâ€ were used to search the literature available from public databases such as â€œPubMedâ€,

â€œPubMed Centralâ€ â€œGoogle Scholarâ€, â€œScience Directâ€ and â€œScopusâ€ and the same is checked for removing repetitions. The data was extracted and collected literature was thoroughly analysed. SCD/SCA is a commonly prevalent hereditary hemoglobinopathy disease and is related to augmented risk factors and premature mortality. Results: SCD severely affects pregnancy, which leads to the elevated occurrence of perinatal and maternal outcomes such as pre-eclampsia, eclampsia, abortions, intrauterine growth retardation (IUGR), etc., and sufficient care during the pregnancy guarantees an improved outcome. Due to the best health care conveniences, availability of drugs such as hydroxyurea, antibiotic prophylaxis, and vaccination, the life expectancy of SCD patients has greatly improved in recent times though directly related to the access and services available at the healthcare facilities for the needy and poor. Moreover, the latest innovations in the fields of prenatal screening and preimplantation genetic diagnosis (PGD), facilitate partners suffering from SCA/SCD to have a healthy child. There are no available studies on the prevalence of SCA/SCD in pregnant women among ethnic tribal populations from India. Conclusion: This review article is focused on the effects of SCA/SCD on pregnancy outcomes, the consistent follow-up, routine check-ups and successful management of complications throughout pregnancy, the various diagnostic methods toward preventive methods, curative and management therapeutic strategies and also defines the perinatal and maternal outcomes in the ethnic tribal populations of India.

29. **The effects of old and recent migration waves in the distribution of HBB*S globin gene haplotypes.**

    2016

    Genetics and molecular biology

    Lindenau, Juliana D and Wagner, Sandrine C and Castro, Simone M de and Hutz, Mara H

Sickle cell hemoglobin is the result of a mutation at the sixth amino acid position of the beta (Î²) globin chain. The HBB*S gene is in linkage disequilibrium with five main haplotypes in the Î²-globin-like gene cluster named according to their ethnic and geographic origins: Bantu (CAR), Benin (BEN), Senegal (SEN), Cameroon (CAM) and Arabian-Indian (ARAB). These haplotypes demonstrated that the sickle cell mutation arose independently at least five times in human history. The distribution of Î²S haplotypes among Brazilian populations showed a predominance of the CAR haplotype. American populations were clustered in two groups defined by CAR or BEN haplotype frequencies. This scenario is compatible with historical records about the slave trade in the Americas. When all world populations where the sickle cell gene occurs were analyzed, three clusters were disclosed based on CAR, BEN or ARAB haplotype predominance. These patterns may change in the next decades due to recent migrations waves. Since these haplotypes show different clinical characteristics, these recent migrations events raise the necessity to develop optimized public health programs for sickle cell disease screening and management.

30. **Haemoglobinopathies in the Indian subcontinent. A review of literature.**

    1973

    Acta geneticae medicae et gemellologiae

    Saha, N and Banerjee, B

31. **Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013**

    2015

    The Lancet

Up-to-date evidence on levels and trends for age-sex-specific all-cause and cause-specific mortality is essential for the formation of global, regional, and national health policies. In the Global Burden of Disease Study 2013 (GBD 2013) we estimated yearly deaths for 188 countries between 1990, and 2013. We used the results to assess whether there is epidemiological convergence across countries. Methods

We estimated age-sex-specific all-cause mortality using the GBD 2010 methods with some refinements to improve accuracy applied to an updated database of vital registration, survey, and census data. We generally estimated cause of death as in the GBD 2010. Key improvements included the addition of more recent vital registration data for 72 countries, an updated verbal autopsy literature review, two new and detailed data systems for China, and more detail for Mexico, UK, Turkey, and Russia. We improved statistical models for garbage code redistribution. We used six different modelling strategies across the 240 causes; cause of death ensemble modelling (CODEm) was the dominant strategy for causes with sufficient information. Trends for Alzheimer's disease and other dementias were informed by meta-regression of prevalence studies. For pathogen-specific causes of diarrhoea and lower respiratory infections we used a counterfactual approach. We computed two measures of convergence (inequality) across countries: the average relative difference across all pairs of countries (Gini coefficient) and the average absolute difference across countries. To summarise broad findings, we used multiple decrement life-tables to decompose probabilities of death from birth to exact age 15 years, from exact age 15 years to exact age 50 years, and from exact age 50 years to exact age 75 years, and life expectancy at birth into major causes. For all quantities reported, we computed 95% uncertainty intervals (UIs). We constrained cause-specific fractions within each age-sex-country-year group to sum to all-cause mortality based on draws from the uncertainty distributions. Findings - Global life expectancy for both sexes increased from 65Â·3 years (UI 65Â·0-65Â·6) in 1990, to 71Â·5 years (UI 71Â·0-71Â·9) in 2013, while the number of deaths increased from 47Â·5 million (UI 46Â·8-48Â·2) to 54Â·9 million (UI 53Â·6-56Â·3) over the same interval. Global progress masked variation by age and sex: for children, average absolute differences between countries decreased but relative differences increased. For women aged 25-39 years and older than 75 years and for men aged 20-49 years and 65 years and older, both absolute and relative differences increased. Decomposition of global and regional life expectancy showed the prominent role of reductions in age-standardised death rates for cardiovascular diseases and cancers in high-income regions, and reductions in child deaths from diarrhoea, lower respiratory infections, and neonatal causes in low-income regions. HIV/AIDS reduced life expectancy in southern sub-Saharan Africa. For most communicable causes of death both numbers of deaths and age-standardised death rates fell whereas for most non-communicable causes, demographic shifts have increased numbers of deaths but decreased age-standardised death rates. Global deaths from injury increased by 10Â·7%, from 4Â·3 million deaths in 1990 to 4Â·8 million in 2013; but age-standardised rates declined over the same period by 21%. For some causes of more than 100 000 deaths per year in 2013, age-standardised death rates increased between 1990 and 2013, including HIV/AIDS, pancreatic cancer, atrial fibrillation and flutter, drug use disorders, diabetes, chronic kidney disease, and sickle-cell anaemias. Diarrhoeal diseases, lower respiratory infections, neonatal causes, and malaria are still in the top five causes of death in children younger than 5 years. The most important pathogens are rotavirus for diarrhoea and pneumococcus for lower respiratory infections. Country-specific probabilities of death over three phases of life were substantially varied between and within regions. Interpretation - For most countries, the general pattern of reductions in age-sex specific mortality has been associated with a progressive shift towards a larger share of the remaining deaths caused by non-communicable disease and injuries. Assessing epidemiological convergence across countries depends on whether an absolute or relative measure of inequality is used. Nevertheless, age-standardised death rates for seven substantial causes are increasing, suggesting the potential for reversals in some countries. Important gaps exist in the empirical data for cause of death estimates for some countries; for example, no national data for India are available for the past decade. Funding - Bill & Melinda Gates Foundation.

32. Situational Analysis of Sickle Cell Disease in Gujarat, India.

2017

Indian Journal of Community Medicine

Saxena, Deepak and Yasobant, Sandul and Golechha, Mahaveer

Background: Sickle cell disease (SCD) is a major public health concern in tribal community not only in Gujarat but also globally. Gujarat, a western state of India, has 89.12 lakh tribal populations and is expected to have at least 9,00,000 sickle cell trait and 70,000 SCD patients. The aim of the present review is to document the prevalence of SCD in various communities and various screening methods adapted. Methodology: An in-depth

literature review was carried out using available search engines such as Cochrane Library, PubMed, Scopus etc. and published articles, and government reports/policy documents with reference to SCD were gathered. Results: A total of 17 original research articles and 2 policy/program documents are included in this review. The review suggests a prevalence of 0.6%-35% studies conducted among medical students, tribal schoolchildren, and tribal adolescents, with diverse screening methodologies. Conclusion: A diverse prevalence is observed in this review. Various screening methods such as dithionite turbidity test/hemoglobin/high-performance liquid chromatography methods were used to estimate the prevalence, citing the need for standardization. It was also found that not only tribal population, but also nontribal population have the risk of getting SCD that needs to be further investigated properly. Qualitative studies with SCD patients are required to understand the quality of life and morbidity pattern.

33. Thalassemia and related hemoglobinopathies.

2005

Indian Journal of Pediatrics

SA, Sarnaik and Sarnaik, Sharada A

Hemoglobinopathies are the most common single gene disorders in man. There are several hundred of these disorders though the thalassemias -- alpha and beta and the sickling disorders make up the vast majority. Recent advances in the understanding of the hemoglobin structure and the genetics of its synthesis has contributed significantly to the understanding of these diseases. Disorders include those with reduced globin synthesis, abnormal globin chains and failure to switch globin chain synthesis at the appropriate age. This review focuses on the clinical features, diagnosis and management strategies of the alpha and beta thalassemias, the sickling disorders and touches on a few rarer hemoglobinopathies. It also emphasizes prevention strategies and chronic transfusion safety in countries like India where there are limited resources.

34. The phenotypic and molecular diversity of hemoglobinopathies in India: A review of 15Â years at a referral center.

2019

International Journal of Laboratory Hematology

Nadkarni, Anita H and Gorakshakar, Ajit C and Sawant, Pratibha M and Italia, Khushnooma Y and Upadhye, Dipti S and Gorivale, Manju S and Mehta, Pallavi R and Hariharan, Priya and Ghosh, Kanjaksha and Colah, Roshan B

Introduction: The hemoglobinopathies pose a significant health burden in India. Apart from the Î² thalassemias and sickle cell disorders, Î± thalassemias and structural hemoglobin variants are also common. Here we have reviewed the phenotypic and molecular diversity of hemoglobinopathies encountered at a referral center in western India over a period of 15Â years. Materials and Methods: Screening for hemoglobinopathies was done using HPLC and cellulose acetate electrophoresis. Molecular characterization was done using Covalent Reverse Dot Blot Hybridization (CRDB), Amplification Refractory Mutation System (ARMS), GAP PCR and direct DNA sequencing. Results: The study includes 31Â 075 individuals who were referred for diagnosis of hemoglobinopathies and prenatal diagnosis. Of these 14Â 423 individuals showed various hemoglobin abnormalities. Beta genotyping in 5615 individuals showed the presence of 49 Î² thalassemia mutations. 143 Î² thalassemia heterozygotes had normal or borderline HbA2 levels. We identified three Î´ gene mutations (HbA2 Pellendri, HbA2 St.George, HbA2 Saurashtra) in Î² thalassemia heterozygotes leading to normal HbA2 levels. The commonest defects among the raised Hb F determinants were GÎ³(Î‘Î³Î´Î²)0 Indian inversion and the HPFHâ€3 Indian deletion. A total of 312 individuals showed the presence of Î± thalassemia, of which 12.0% had a single Î± gene deletion (âˆ’Î±/Î±Î±). HbH disease was identified in 29 cases with 10 different genotypes. Alpha globin gene triplication was seen in 2.1% of Î² thalassemia heterozygotes with a thalassemia intermedia phenotype. Seven unusual Î± chain variants and eight uncommon Î² chain variants were identified. Conclusion: The repertoire of molecular defects seen in the different globin genes will be valuable for management and control

of these disorders both in India as well as in other countries where there is a huge influx of migrant populations from India.

35. Sickle cell disease in India

2014

Current Opinion in Hematology

Colah, Roshan and Mukherjee, Malay and Ghosh, Kanjaksha

PURPOSE OF REVIEW: Sickle cell disease (SCD) poses a considerable health burden in India. This review focuses on the recent initiatives to understand the variable phenotypes, the role of hydroxyurea in patients with the Asian haplotype and the feasibility of newborn screening, awareness and control programs. RECENT FINDINGS: A systematic long follow up of patients in central India has documented the clinical events and the causes of significant morbidity and mortality. Fixed low dose hydroxyurea was sufficient for a clinical and hematological response in severe patients who had high baseline fetal hemoglobin (HbF) levels. Follow-up of birth cohorts of SCD babies initiated recently has shown that in central India babies clinically present with early and severe anemia, requiring blood transfusions, and septicemia, which are the most common complications, whereas babies from tribal communities in south Gujarat have no severe complications. Greater awareness has led to increasing requests for prenatal diagnosis. SUMMARY: SCD in India is not uniformly mild despite high fetal hemoglobin levels. The benefits of comprehensive care and hydroxyurea therapy have been demonstrated. Newborn screening is acceptable and is beginning to throw light on the natural history of the disease. The central and state governments are now supporting the establishment of centers for the diagnosis of patients and comprehensive care.

36. Doctors for Tribal Areas: Issues and Solutions.

2016

Indian Journal of Community Medicine

Mavalankar, Dileep

Health parameters of tribal population had always been a concern for India's march towards Millennium development Goals (MDG's). Tribal population contributes 8.6% of total population, in spite of efforts and commitment of Government of India towards MGD, India lagged far behind from achieving and optimal health of tribal population will be a concern for achieving Sustainable development Goals SDG's also. Some of the common health problems of the tribal population face are deficiency of essential components in diet like energy malnutrition, protein calorie malnutrition and micronutrient deficiencies. Goiter, Gastrointestinal disorders, particularly dysentery and parasitic infections are very common. High prevalence of genetic disorders like sickle cell anemia and others are endemic in few tribes of India. Tribal Health is further compounded issues by social issues like excessive consumption of alcohol, poor access to contraceptive, substance abuse and gender based violence. Besides other reasons, like poor budget allocation, difficult to reach, poor access to health care facility, severe shortage of qualified health workers and workforce led to poor governance of health sector in tribal areas. Present view point reflects on the issues of inadequacy of doctors in tribal area and suggests possible solutions.

37. Clinical manifestations of sickle cell disease in India: misconceptions and reality.

2018

Current Opinion in Hematology

Jain, Dipty and Mohanty, Dipika

Purpose Of Review: In the past, milder clinical manifestations of sickle cell disease (SCD) have been described from India. However, recent data from some parts of India suggest that the severity of the disease can be compared to that of African phenotypes. This review therefore describes the varied clinical manifestation of SCD, the

success of newborn screening programme, prenatal diagnosis and low dose hydroxyurea therapy in India.Recent Findings: The varied clinical manifestations such as anemia, vaso-occlusive crisis, acute chest syndrome, renal involvement, stroke and so on vary from one part of the country to the other and also among different communities of India. Strategies for improving quality of life and controlling of SCD have been suggested. Certain factors other than genetics also play an important role in clinical manifestation of the disorder.Summary: The clinical diversity of SCD is described. The natural history of SCD in India is unfolding from newborn screening programme. The use of low-dose hydroxy urea therapy both in adults and children has brought down the incidences of crisis and provides great relief to the patients. The tailor-made programme for India as regards the control and management has been discussed.

38. Differences in the clinical and genotypic presentation of sickle cell disease around the world.

2014

Paediatric Respiratory Reviews

Saraf, Santosh L and Molokie, Robert E and Nouraie, Mehdi and Sable, Craig A and Luchtman-Jones, Lori and Ensing, Gregory J and Campbell, Andrew D and Rana, Sohail R and Niu, Xiao M and Machado, Roberto F and Gladwin, Mark T and Gordeuk, Victor R

Sickle cell disease (SCD), caused by a mutation in the Î²-globin gene HBB, is widely distributed in malaria endemic regions. Cardiopulmonary complications are major causes of morbidity and mortality. Hemoglobin SS (Hb SS) represents a large proportion of SCD in the Americas, United Kingdom, and certain regions of Africa while higher proportions of hemoglobin SC are observed in Burkina Faso and hemoglobin SÎ²-thalassemia in Greece and India. Coinheritance of Î±-thalassemia and persistence of hemoglobin F production are observed in highest frequency in certain regions of India and the Middle East. As confirmed in the PUSH and Walk-PHaSST studies, Hb SS, absence of co-inheriting alpha-thalassemia, and low hemoglobin F levels tend to be associated with more hemolysis, lower hemoglobin oxygen saturations, greater proportions of elevated tricuspid regurgitant jet velocity and brain natriuretic peptide, and increased left ventricular mass index. Identification of additional genetic modifiers will improve prediction of cardiopulmonary complications in SCD.

39. Red blood cell transfusion to treat or prevent complications in sickle cell disease: an overview of Cochrane reviews

2018

Cochrane Database of Systematic Reviews

Fortin PM, Hopewell S and Estcourt, L J

Abstract - Background Globally, sickle cell disease (SCD) is one of the commonest severe monogenic disorders, due to the inheritance of two abnormal haemoglobin (beta globin) genes. SCD can cause severe pain, significant endâ€organ damage, pulmonary complications, and premature death. Red blood cell (RBC) transfusions are used to treat complications of SCD, e.g. acute chest syndrome (ACS) (this often involves a single transfusion episode), or they can be part of a regular longâ€term transfusion programme to prevent SCD complications. Objectives To summarize the evidence in Cochrane Reviews of the effectiveness and safety of RBC transfusions versus no transfusion, or restrictive (to increase the total haemoglobin) versus liberal (to decrease the haemoglobin S level below a specified percentage) transfusion, for treating or preventing complications experienced by people with SCD. Methods We included Cochrane Reviews of randomised or quasiâ€randomised controlled trials published in the Cochrane Database of Systematic Reviews, that addressed various SCD complications and had RBC transfusion as an intervention or comparator. We assessed the methodological quality of included reviews according to the AMSTAR quality assessment. Main results We included 15 Cochrane Reviews, 10 of which had no included studies with an RBC transfusion intervention (five reported RCTs with other interventions; and five contained no studies). Five of the 15 reviews included participants randomised to RBC transfusion, but in one of

these reviews only 10 participants were randomised with no usable data. Four reviews (nine trials with 1502 participants) reported data comparing shortâ€ or longâ€term RBC transfusions versus standard care, diseaseâ€modifying agents, a restrictive versus a liberal transfusion strategy and longâ€term RBC transfusions versus transfusions to treat complications. All reviews were of high quality according to AMSTAR quality assessment, however, the quality of the included trials was highly variable across outcomes. Trials were downgraded according to GRADE methodology for risk of bias, indirectness (most trials were conducted in children with HbSS), and imprecision (outcomes had wide confidence intervals). In all four reviews and all comparisons there was little or no difference in the risk of death (very lowâ€quality evidence). There were either no deaths or death was a rare event. Shortâ€term RBC transfusion versus standard care (one review: two trials, 434 participants, GRADE very lowâ€ to lowâ€quality evidence)â€¨In people undergoing lowâ€ to mediumâ€risk surgery, RBC transfusions may decrease the risk of acute chest syndrome (ACS) in people with African haplotypes compared to standard care (lowâ€quality evidence), but there was little or no difference in people with the Arabic haplotype (veryâ€low quality evidence). There was also little or no difference in the risk of other SCDâ€related or transfusionâ€related complications (veryâ€low quality evidence). Longâ€term RBC transfusion versus standard care (two reviews: three trials, 405 participants, very lowâ€ to moderateâ€quality evidence)â€¨In children and adolescents at high risk of stroke (abnormal transcranial doppler (TCD) velocities or silent cerebral infarct (SCI)), longâ€term RBC transfusions probably decrease the risk of stroke (moderateâ€quality evidence) and may decrease the risk of ACS and painful crisis compared to standard care (lowâ€quality evidence). Longâ€term RBC transfusions may also decrease the risk of SCI in children with abnormal TCD velocities (lowâ€quality evidence), but there may be little or no difference in the risk of SCI in children with normal TCD velocities and previous SCI (lowâ€quality evidence). In children and adolescents already receiving longâ€term RBC transfusions for preventing stroke, in comparison to standard care, continuing longâ€term RBC transfusions may reduce the risk of SCI (lowâ€quality evidence) but we do not know whether there is a difference in the risk of stroke (veryâ€low quality evidence). In children with normal TCD velocities and SCI there was little or no difference in the risk of alloimmunisation or transfusion reactions, but RBC transfusions may increase the risk of iron overload (lowâ€quality evidence). Longâ€term RBC transfusion versus RBC transfusion to treat complications (one review: one trial, 72 participants, very lowâ€ to lowâ€quality evidence)â€¨In pregnant women, longâ€term RBC transfusions may decrease the risk of painful crisis compared to transfusion for complications (lowâ€quality evidence); but there may be little or no difference in the risk of other SCDâ€related complications or transfusion reactions (veryâ€low quality evidence). RBC transfusion versus diseaseâ€modifying agents (hydroxyurea) (two reviews: two trials; 254 participants, very lowâ€ to lowâ€quality evidence)â€¨For primary prevention of stroke in children, with abnormal TCD and no severe vasculopathy on magnetic resonance imaging/magnetic resonance angiography (MRI/MRA), who have received at least one year of RBC transfusions, we do not know whether there is a difference between RBC transfusion and diseaseâ€modifying agents in the risk of stroke; SCI; ACS; or painful crisis (veryâ€low quality evidence). There may be little or no difference in the risk of iron overload (lowâ€quality evidence). Similarly, for secondary prevention of stroke in children and adolescents, we do not know whether there is a difference between these interventions in the risk of stroke; SCI; or ACS (veryâ€low quality evidence); but hydroxyurea with phlebotomy may increase the risk of painful crisis and global SCD serious adverse events compared to RBC transfusion (lowâ€quality evidence). There may be little or no difference in the risk of iron overload (lowâ€quality evidence). Restrictive versus liberal RBC transfusion strategy (one review: one trial; 230 participants, very lowâ€quality evidence)â€¨In people undergoing cholecystectomy, there was little or no difference between strategies in the risk of SCDâ€related or transfusionâ€related complications (veryâ€low quality evidence). Authors' conclusions This overview provides support from two highâ€quality Cochrane Reviews for the use of RBC transfusions in preventing stroke in children and adolescents at high risk of stroke (abnormal TCDs or SCI) and evidence that it may decrease the risk of SCI in children with abnormal TCD velocities. In addition RBC transfusions may reduce the risk of ACS and painful crisis in this population. This overview highlights the lack of highâ€quality evidence in adults with SCD and the number of reviews that have no evidence for the use of RBC transfusions across a spectrum of SCD complications. Also of concern is the variable and often incomplete reporting of patientâ€relevant outcomes in the included trials such as

SCDâ€relatedserious adverse events and quality of life. Plain language summary An overview of Cochrane Reviews on red blood cell transfusions to treat or prevent sickle cell diseaseâ€related complications Review question To summarize the evidence in Cochrane Reviews of the effectiveness and safety of red blood cell (RBC) transfusions for treating or preventing complications experienced by people with sickle cell disease (SCD). Background SCD is a serious inherited blood disorder where the RBCs, which carry oxygen around the body, develop abnormally. Normal RBCs are flexible and discâ€shaped, but in SCD they can become rigid and crescent shaped. Sickled cells are not only less flexible than healthy RBCs, they are also stickier. This can lead to the blockage of blood vessels, resulting in tissue and organ damage and episodes of severe pain. The abnormal RBCs are more fragile and break apart, which leads to fewer of them, known as anaemia. Overview characteristics We searched for Cochrane Reviews that analysed the data from randomised controlled trials (RCT; experiments that randomly allocate participants to one of two or more treatment groups), which looked at the effectiveness of RBC transfusions to prevent or treat SCD complications. This overview summarises the results of these reviews. Key results 15 reviews met the inclusion criteria for this overview. However, only four reviews (which included nine RCTs and 1052 participants) looked at the effects of RBCtransfusion and had results that could be reported. In the four reviews there was no difference in the risk of death with any comparison. We found that longâ€termRBC transfusions compared to standard care, probably decrease the risk of stroke in children and adolescents at high risk of stroke (abnormal transcranial doppler (TCD) ultrasound (high blood flow to the brain) or a previous silent stroke (a stroke with no outward symptoms and where a person is typically unaware they have suffered a stroke)) and may also decrease their risk of painful crisis and acute chest syndrome. Red blood cell transfusions may also decrease the risk of silent stroke in children with abnormal TCD ultrasound when compared to standard care. We found there was a lack of evidence for treating adults with SCDâ€relatedcomplications and that important outcomes, including quality of life were often not measured or reported. Quality of the reviews and evidence within reviews All reviews included in this review were of high quality and met Cochrane standards for systematic reviews. However, the quality of the trials included in the reviews was variable across the trials and in relation to the outcomes. The quality of the evidence within the trials was downgraded because trials had a high risk of bias, outcomes had imprecise measurements and much of the evidence applied only to children with HbSS disease. People with SCD are living longer and we need more highâ€quality evidence on treating adults with SCD; as well as on the best treatment options, including the role of RBC transfusions, to treat SCD complications. We also need to improve and standardise the reporting of outcomes across trials.

40. Regular longâ€term red blood cell transfusions for managing chronic chest complications in sickle cell disease

2019

Cochrane Database of Systematic Reviews

Estcourt LJ, Hopewell S Trivella M Hambleton I R and Cho, G

Abstract - Background Sickle cell disease is a genetic haemoglobin disorder, which can cause severe pain, significant endâ€organ damage, pulmonary complications, and premature death. Sickle cell disease is one of the most common severe monogenic disorders in the world, due to the inheritance of two abnormal haemoglobin (beta globin) genes. The two most common chronic chest complications due to sickle cell disease are pulmonary hypertension and chronic sickle lung disease. These complications can lead to morbidity (such as reduced exercise tolerance) and increased mortality. This is an update of a Cochrane Review first published in 2011 and updated in 2014 and 2016. Objectives We wanted to determine whether trials involving people with sickle cell disease that compare regular longâ€termblood transfusion regimens with standard care, hydroxycarbamide (hydroxyurea) any other drug treatment show differences in the following: mortality associated with chronic chest complications; severity of established chronic chest complications; development and progression of chronic chest complications; serious adverse events. Search methods We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register. Date of the last search: 19 September 2019. We also searched for randomised controlled trials in the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, Issue 10, 14 November 2018), MEDLINE (from 1946), Embase (from 1974), CINAHL (from 1937), the

Transfusion Evidence Library (from 1950), and ongoing trial databases to 14 November 2018. Selection criteria We included randomised controlled trials of people of any age with one of four common sickle cell disease genotypes, i.e. Hb SS, SÎ²Âº, SC, or SÎ² + that compared regular red blood cell transfusion regimens (either simple or exchange transfusions) to hydroxycarbamide, any other drug treatment, or to standard care that were aimed at reducing the development or progression of chronic chest complications (chronic sickle lung and pulmonary hypertension). Data collection and analysis We used the standard methodological procedures expected by Cochrane. Main results No studies matching the selection criteria were found. Authors' conclusions There is a need for randomised controlled trials looking at the role of longâ€term transfusion therapy in pulmonary hypertension and chronic sickle lung disease. Due to the chronic nature of the conditions, such trials should aim to use a combination of objective and subjective measures to assess participants repeatedly before and after the intervention. Plain language summary The effect of longâ€term red blood cell transfusions on chronic chest complications of sickle cell disease Review question We reviewed the evidence to see if regular longâ€term red blood cell transfusions helped to reduce the occurrence or progression of chronic chest complications compared to hydroxycarbamide (hydroxyurea), any other treatment or standard care in people with sickle cell disease. This is an update of a previously published Cochrane Review. Background Oxygen is transported from our lungs to all parts of our body by haemoglobin, which is a major component of red blood cells. Sickle cell disease is an inherited disorder of haemoglobin. In people with sickle cell disease red blood cells become rigid once they have given up their oxygen and are often shaped like crescents. These rigid cells can block blood vessels, which causes problems throughout the body, including the lungs. The two most common chronic chest complications due to sickle cell disease are pulmonary hypertension and chronic sickle lung disease. Pulmonary hypertension is high blood pressure in the pulmonary arteries (the arteries that supply blood to the lungs). High blood pressure in these arteries are associated with an increased risk of death. Chronic sickle lung disease arises as a result of lung damage and loss of lung tissue. Regular blood transfusions for people with sickle cell disease reduce the amount of the person's own sickled cells in their blood by replacing them with donated, nonâ€sickled cells. Regular transfusions have already been shown to reduce the risk of strokes in people with sickle cell disease. We aimed to find out if regular longâ€term blood transfusions in people with this disease lead to a reduction in new chronic chest complications or slowed the progression of any chronic chest complications that have already developed. We also aimed to consider death rates due to chronic chest complications and any adverse effects of the transfusion programme. Study characteristics The evidence is current to 19 September 2019. We found no studies in this update of the review. Key results There are no results because we found no relevant randomised controlled trials. We would need to design a study with at least 946 participants to be able to detect a decrease in the number of people who died from 12 in 100 to six in 100. Quality of the evidence There is no evidence from randomised controlled trials to answer our review questions.

41. Zinc supplements for treating thalassaemia and sickle cell disease

2013

Cochrane Database of Systematic Reviews

Swe KMM, Abas A B L Bhardwaj A Barua A and Nair, N S and Swe, K M M and Abas, A B L and Bhardwaj, A and Barua, A and Nair, N S

Background: Haemoglobinopathies, inherited disorders of haemoglobin synthesis (thalassaemia) or structure (sickle cell disease), are responsible for significant morbidity and mortality throughout the world. The WHO estimates that, globally, 5% of adults are carriers of a haemoglobin condition, 2.9% are carriers of thalassaemia and 2.3% are carriers of sickle cell disease. Carriers are found worldwide as a result of migration of various ethnic groups to different regions of the world. Zinc is an easily available supplement and intervention programs have been carried out to prevent deficiency in people with thalassaemia or sickle cell anaemia. It is important to evaluate the role of zinc supplementation in the treatment of thalassaemia and sickle cell anaemia to reduce deaths due to complications. Objectives: To assess the effect of zinc supplementation in the treatment of thalassaemia and sickle cell disease. Search methods: We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register comprising references identified from comprehensive electronic database

searches and handsearches of relevant journals and abstract books of conference proceedings. Date of most recent search: 01 February 2013. Selection criteria: Randomised, placebo-controlled trials of zinc supplements for treating thalassaemia or sickle cell disease administered at least once a week for at least a month. Data collection and analysis: Two review authors assessed the eligibility and risk of bias of the included trials, extracted and analysed data and wrote the review. We summarised results using risk ratios or rate ratios for dichotomous data and mean differences for continuous data. We combined trial results where appropriate. Main results: We identified nine trials for inclusion with all nine contributing outcome data. Two trials reported on people with thalassaemia (n = 152) and seven on sickle cell anaemia (n = 307). In people with thalassaemia, in one trial, the serum zinc level value showed no difference between the zinc supplemented group and the control group, mean difference 47.40 (95% confidence interval -12.95 to 107.99). Regarding anthropometry, in one trial, height velocity was significantly increased in patients who received zinc supplementation for one to seven years duration, mean difference 3.37 (95% confidence interval 2.36 to 4.38) (total number of participants = 26). In one trial, however, there was no difference in body mass index between treatment groups. Zinc acetate supplementation for three months (in one trial) and one year (in two trials) (total number of participants = 71) was noted to increase the serum zinc level significantly in patients with sickle cell anaemia, mean difference 14.90 (95% confidence interval 6.94 to 22.86) and 20.25 (95% confidence interval 11.73 to 28.77) respectively. There was no significant difference in haemoglobin level between intervention and control groups, at either three months (one trial) or one year (one trial), mean difference 0.06 (95% confidence interval -0.84 to 0.96) and mean difference -0.07 (95% confidence interval -1.40 to 1.26) respectively. Regarding anthropometry, one trial showed no significant changes in body mass index or weight after one year of zinc acetate supplementation. In patients with sickle cell disease, the total number of sickle cell crises at one year were significantly decreased in the zinc sulphate supplemented group as compared to controls, mean difference -2.83 (95% confidence interval -3.51 to -2.15) (total participants 130), but not in zinc acetate group, mean difference 1.54 (95% confidence interval -2.01 to 5.09) (total participants 22). In one trial at three months and another at one year, the total number of clinical infections were significantly decreased in the zinc supplemented group as compared to controls, mean difference 0.05 (95% confidence interval 0.01 - 0.43) (total number of participants = 36), and mean difference -7.64 (95% confidence interval -10.89 to -4.39) (total number of participants = 21) respectively. Authors' conclusions: According to the results, there is no evidence from randomised controlled trials to indicate any benefit of zinc supplementation with regards to serum zinc level in patients with thalassaemia. However, height velocity was noted to increase among those who received this intervention. There is mixed evidence on the benefit of using zinc supplementation in people with sickle cell disease. For instance, there is evidence that zinc supplementation for one year increased the serum zinc levels in patients with sickle cell disease. However, though serum zinc level was raised in patients receiving zinc supplementation, haemoglobin level and anthropometry measurements were not significantly different between groups. Evidence of benefit is seen with the reduction in the number of sickle cell crises among sickle cell patients who received one year of zinc sulphate supplementation and with the reduction in the total number of clinical infections among sickle cell patients who received zinc supplementation for both three months and for one year. The conclusion is based on the data from a small group of trials,which were generally of good quality, with a low risk of bias. The authors recommend that more trials on zinc supplementation in thalassaemia and sickle cell disease be conducted given that the literature has shown the benefits of zinc in these types of diseases.

42. CLINICAL REVIEW: Haemoglobinopathies

2006

GP

Provan, Drew

This is mostly because sickled red cells do not flow well through small blood vessels. This leads to blockage of the blood vessels and sickle cell crises. The carriers of the sickle gene are said to have the sickle cell trait, and have red cells that contain a mixture of normal HbA and sickle haemoglobin S (HbAS). Sickle cell carriers are not anaemic and have no clinical abnormalities.

43. Erythrophagocytosis in sickle cell anemia: Statistical evidence for a biological phenomenon

2007

Medical Hypotheses

Mamtani, M and Sharma, M and Amin, M and Amin, A and Jawahirani, A and Kulkarni, H

The precise role of erythrophagocytosis in sickle cell disease is not known. Using hematological data from three studies and 791 subjects comprising of eight epidemiological groups, we found a strong statistical support for the hypothesis that erythrophagocytosis is increased in sickle cell trait, that neutrophils and lymphocytes are the most likely cells involved in erythrophagocytosis in these subjects and that increased erythrophagocytosis may for a mechanistic explanation for an increased risk of vaso-occlusive crisis in sickle cell trait. Statistically, erythrophagocytosis was not increased in subjects with homozygous sickle cell disease. Our findings offer an interesting mechanistic implication about the presence of a strong autoimmune component of sickle cell trait that can be explained by the well recognized interplay between the receptor molecule signal regulatory protein-Î± (SIRP-Î±) on the phagocyte and its ligand, CD47, on the red blood cell. Our findings also support further and closer evaluation of the other hypothesized mechanisms by which neutrophils and lymphocytes partake in differential degree of erythrophagocytosis in subjects heterozygous for the sickle hemoglobin. Finally, translation of these findings into a clinical realm suggests that the extent of erythrophagocytosis, as measured by peripheral blood hematological indicators, can serve as an important indicator of the likelihood of future vaso-occlusive crisis events in subjects of sickle cell trait. Â© 2006 Elsevier Ltd. All rights reserved.

44. Free heme toxicity and its detoxification systems in human

2005

Toxicology Letters

Kumar, S and Bandyopadhyay, U

Severe hemolysis or myolysis occurring during pathological states, such as sickle cell disease, ischemia reperfusion, and malaria results in high levels of free heme, causing undesirable toxicity leading to organ, tissue, and cellular injury. Free heme catalyzes the oxidation, covalent cross-linking and aggregate formation of protein and its degradation to small peptides. It also catalyzes the formation of cytotoxic lipid peroxide via lipid peroxidation and damages DNA through oxidative stress. Heme being a lipophilic molecule intercalates in the membrane and impairs lipid bilayers and organelles, such as mitochondria and nuclei, and destabilizes the cytoskeleton. Heme is a potent hemolytic agent and alters the conformation of cytoskeletal protein in red cells. Free heme causes endothelial cell injury, leading to vascular inflammatory disorders and stimulates the expression of intracellular adhesion molecules. Heme acts as a pro-inflammatory molecule and heme-induced inflammation is involved in the pathology of diverse conditions; such as renal failure, arteriosclerosis, and complications after artificial blood transfusion, peritoneal endometriosis, and heart transplant failure. Heme offers severe toxic effects to kidney, liver, central nervous system and cardiac tissue. Although heme oxygenase is primarily responsible to detoxify free heme but other extra heme oxygenase systems also play a significant role to detoxify heme. A brief account of free heme toxicity and its detoxification systems along with mechanistic details are presented. Â© 2005 Elsevier Ireland Ltd. All rights reserved.

45. Erythrocyte and platelet proteomics in hematological disorders

2016

Proteomics - Clinical Applications

Chakrabarti, A and Halder, S and Karmakar, S

Erythrocytes undergo ineffective erythropoesis, hemolysis, and premature eryptosis in sickle cell disease and thalassemia. Abnormal hemoglobin variants associated with hemoglobinopathy lead to vesiculation, membrane instability, and loss of membrane asymmetry with exposal of phosphatidylserine. This potentiates thrombin generation resulting in activation of the coagulation cascade responsible for subclinical phenotypes. Platelet activation also results in the release of microparticles, which express and transfer functional receptors from platelet membrane, playing key roles in vascular reactivity and activation of intracellular signaling pathways. Over the last decade, proteomics had proven to be an important field of research in studies of blood and blood diseases. Blood cells and its fluidic components have been proven to be easy systems for studying differential expressions of proteins in hematological diseases encompassing hemoglobinopathies, different types of anemias, myeloproliferative disorders, and coagulopathies. Proteomic studies of erythrocytes and platelets reported from several groups have highlighted various factors that intersect the signaling networks in these anucleate systems. In this review, we have elaborated on the current scenario of anucleate blood cell proteomes in normal and diseased individuals and the cross-talk between the two major constituent cell types of circulating blood.

46. Blood transfusions for treating acute chest syndrome in people with sickle cell disease

2020

Cochrane Database of Systematic Reviews

Dolatkhah, R and Dastgiri, S

Abstract - Background Sickle cell disease is an inherited autosomal recessive blood condition and is one of the most prevalent genetic blood diseases worldwide. Acute chest syndrome is a frequent complication of sickle cell disease, as well as a major cause of morbidity and the greatest single cause of mortality in children with sickle cell disease. Standard treatment may include intravenous hydration, oxygen as treatment for hypoxia, antibiotics to treat the infectious cause and blood transfusions may be given. This is an update of a Cochrane Review first published in 2010 and updated in 2016. Objectives To assess the effectiveness of blood transfusions, simple and exchange, for treating acute chest syndrome by comparing improvement in symptoms and clinical outcomes against standard care. Search methods We searched The Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register, which comprises references identified from comprehensive electronic database searches and handsearching of relevant journals and abstract books of conference proceedings. Date of the most recent search: 30 May 2019. Selection criteria Randomised controlled trials and quasiâ€randomised controlled trials comparing either simple or exchange transfusion versus standard care (no transfusion) in people with sickle cell disease suffering from acute chest syndrome. Data collection and analysis Both authors independently selected trials and assessed the risk of bias, no data could be extracted. Main results One trial was eligible for inclusion in the review. While in the multicentre trial 237 people were enrolled (169 SCC, 42 SC, 15 SÎ²â°â€thalassaemia, 11SÎ² + â€thalassaemia); the majority were recruited to an observational arm and only ten participants met the inclusion criteria for randomisation. Of these, four were randomised to the transfusion arm and received a single transfusion of 7 to 13 mL/kg packed red blood cells, and six were randomised to standard care. None of the four participants who received packed red blood cells developed acute chest syndrome, while 33% (two participants) developed acute chest syndrome in standard care arm. No data for any preâ€defined outcomes were available. Authors' conclusions We found only one very small randomised controlled trial; this is not enough to make any reliable conclusion to support the use of blood transfusion. Whilst there appears to be some indication that chronic blood transfusion may play a roll in reducing the incidence of acute chest syndrome in people with sickle cell disease and albeit offering transfusions may be a widely accepted clinical practice, there is currently no reliable evidence to support or refute the perceived benefits of these as treatment options; very limited information about any of the potential harms associated with these interventions or indeed guidance that can be used to aid clinical decision making. Clinicians should therefore base any treatment decisions on a combination of; their clinical experience, individual circumstances and the unique characteristics and preferences of adequately informed people with sickle cell disease who are suffering with acute chest syndrome. This review highlights the need of further high quality research to provide reliable evidence for the effectiveness of these interventions for the relief of the symptoms of acute chest syndrome in people with sickle cell disease. Plain

language summary Blood transfusions for treating acute chest syndrome in people with sickle cell disease Review question We reviewed the effectiveness of blood transfusions, for treating acute chest syndrome by comparing improvement in symptoms and clinical outcomes against standard care. This is an update of a Cochrane Review first published in 2010 and updated in 2016. Background Sickle cell disease (SCD) is an inherited blood condition affecting over 250 million people worldwide and is particularly common in Subâ€Saharan Africa, South and Central America, Saudi Arabia, India and a number of Mediterranean countries. It is characterized by the presence of sickleâ€shaped red blood cells which are capable of blocking the blood vessels causing pain and severe damage to several organs of the body. People with SCD may have the acute onset of chest problems which may include fever, this is called acute chest syndrome. Treatment will depend on the individuals' clinical condition and the severity of the symptoms. Standard treatment consists of supportive care, antibiotics, intravenous fluids and blood transfusion, either simple or exchange, may also be indicated. Search date The evidence is current to: 30 May 2019. Key results One study was included in the review, there were two parts to the study, one larger observational study and one randomised trial which was to assess transfusion versus standard care to prevent acute chest syndrome in people with sickle cell disease, while twentyâ€six centres were contracted. Only 10 participants were enrolled into the randomised trial. The effects of blood transfusions could not be determined from the trial; there were no data that could be presented or therefore analysed within this review for the very small number of participants enrolled. Therefore, this unique study did not show how effective blood transfusions might be for treating acute chest syndrome in people with sickle cell disease. Future research is needed to provide evidence for people to make informed decisions on whether blood transfusions are effective for treating acute chest syndrome in people with sickle cell disease.

47. Blood transfusion for preventing primary and secondary stroke in people with sickle cell disease

2020

Cochrane Database of Systematic Reviews

Estcourt LJ, Kohli R Hopewell S Trivella M and Wang, W C

Abstract - Background Sickle cell disease is one of the commonest severe monogenic disorders in the world, due to the inheritance of two abnormal haemoglobin (beta globin) genes. Sickle cell disease can cause severe pain, significant endâ€organ damage, pulmonary complications, and premature death. Stroke affects around 10% of children with sickle cell anaemia (HbSS). Chronic blood transfusions may reduce the risk of vasoâ€occlusion and stroke by diluting the proportion of sickled cells in the circulation. This is an update of a Cochrane Review first published in 2002, and last updated in 2017. Objectives To assess risks and benefits of chronic blood transfusion regimens in people with sickle cell disease for primary and secondary stroke prevention (excluding silent cerebral infarcts). Search methods We searched for relevant trials in the Cochrane Library, MEDLINE (from 1946), Embase (from 1974), the Transfusion Evidence Library (from 1980), and ongoing trial databases; all searches current to 8 October 2019. We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register: 19 September 2019. Selection criteria Randomised controlled trials comparing red blood cell transfusions as prophylaxis for stroke in people with sickle cell disease to alternative or standard treatment. There were no restrictions by outcomes examined, language or publication status. Data collection and analysis Two authors independently assessed trial eligibility and the risk of bias and extracted data. Main results We included five trials (660 participants) published between 1998 and 2016. Four of these trials were terminated early. The vast majority of participants had the haemoglobin (Hb)SS form of sickle cell disease. Three trials compared regular red cell transfusions to standard care in primary prevention of stroke: two in children with no previous longâ€term transfusions; and one in children and adolescents on longâ€term transfusion. Two trials compared the drug hydroxyurea (hydroxycarbamide) and phlebotomy to longâ€term transfusions and iron chelation therapy: one in primary prevention (children); and one in secondary prevention (children and adolescents). The quality of the evidence was very low to moderate across different outcomes according to GRADE methodology. This was due to the trials being at a high risk of bias due to lack of blinding, indirectness and imprecise outcome estimates. Red cell transfusions versus standard care Children with no previous longâ€term transfusions Longâ€term transfusions probably reduce the incidence of clinical stroke in children

with a higher risk of stroke (abnormal transcranial doppler velocities or previous history of silent cerebral infarct), risk ratio 0.12 (95% confidence interval 0.03 to 0.49) (two trials, 326 participants), moderate quality evidence. Longâ€term transfusions may: reduce the incidence of other sickle cell diseaseâ€related complications (acute chest syndrome, risk ratio 0.24 (95% confidence interval 0.12 to 0.48)) (two trials, 326 participants); increase quality of life (difference estimate â€0.54, 95% confidence interval â€0.92 to â€0.17) (one trial, 166 participants); but make little or no difference to IQ scores (least square mean: 1.7, standard error 95% confidence interval â€1.1 to 4.4) (one trial, 166 participants), low quality evidence. We are very uncertain whether longâ€term transfusions: reduce the risk of transient ischaemic attacks, Peto odds ratio 0.13 (95% confidence interval 0.01 to 2.11) (two trials, 323 participants); have any effect on allâ€cause mortality, no deaths reported (two trials, 326 participants); or increase the risk of alloimmunisation, risk ratio 3.16 (95% confidence interval 0.18 to 57.17) (one trial, 121 participants), very low quality evidence. Children and adolescents with previous longâ€term transfusions (one trial, 79 participants) We are very uncertain whether continuing longâ€term transfusions reduces the incidence of: stroke, risk ratio 0.22 (95% confidence interval 0.01 to 4.35); or allâ€cause mortality, Peto odds ratio 8.00 (95% confidence interval 0.16 to 404.12), very low quality evidence. Several review outcomes were only reported in one trial arm (sickle cell diseaseâ€related complications, alloimmunisation, transient ischaemic attacks). The trial did not report neurological impairment, or quality of life. Hydroxyurea and phlebotomy versus red cell transfusions and chelation Neither trial reported on neurological impairment, alloimmunisation, or quality of life. Primary prevention, children (one trial, 121 participants) Switching to hydroxyurea and phlebotomy may have little or no effect on liver iron concentrations, mean difference â€1.80 mg Fe/g dryâ€weight liver (95% confidence interval â€5.16 to 1.56), low quality evidence. We are very uncertain whether switching to hydroxyurea and phlebotomy has any effect on: risk of stroke (no strokes); allâ€cause mortality (no deaths); transient ischaemic attacks, risk ratio 1.02 (95% confidence interval 0.21 to 4.84); or other sickle cell diseaseâ€related complications (acute chest syndrome, risk ratio 2.03 (95% confidence interval 0.39 to 10.69)), very low quality evidence. Secondary prevention, children and adolescents (one trial, 133 participants) Switching to hydroxyurea and phlebotomy may: increase the risk of sickle cell diseaseâ€related serious adverse events, risk ratio 3.10 (95% confidence interval 1.42 to 6.75); but have little or no effect on median liver iron concentrations (hydroxyurea, 17.3 mg Fe/g dryâ€weight liver (interquartile range 10.0 to 30.6)); transfusion 17.3 mg Fe/g dryâ€weight liver (interquartile range 8.8 to 30.7), low quality evidence. We are very uncertain whether switching to hydroxyurea and phlebotomy: increases the risk of stroke, risk ratio 14.78 (95% confidence interval 0.86 to 253.66); or has any effect on allâ€cause mortality, Peto odds ratio 0.98 (95% confidence interval 0.06 to 15.92); or transient ischaemic attacks, risk ratio 0.66 (95% confidence interval 0.25 to 1.74), very low quality evidence. Authors' conclusions There is no evidence for managing adults, or children who do not have HbSS sickle cell disease. In children who are at higher risk of stroke and have not had previous longâ€term transfusions, there is moderate quality evidence that longâ€term red cell transfusions reduce the risk of stroke, and low quality evidence they also reduce the risk of other sickle cell diseaseâ€related complications. In primary and secondary prevention of stroke there is low quality evidence that switching to hydroxyurea with phlebotomy has little or no effect on the liver iron concentration. In secondary prevention of stroke there is lowâ€quality evidence that switching to hydroxyurea with phlebotomy increases the risk of sickle cell diseaseâ€related events. All other evidence in this review is of very low quality. Plain language summary Longâ€term blood transfusions to prevent a stroke in people with sickle cell disease Review question We wanted to determine if longâ€term blood transfusions given to people with sickle cell disease who are at a higher risk of stroke (primary prevention) or have had a previous stroke (secondary prevention) decreases their risk of a subsequent stroke without causing severe side effects. We compared longâ€term blood transfusions to standard treatment or other ways of preventing a stroke. This is an update of a previously published Cochrane Review. Interventions for silent stroke are addressed in a separate Cochrane Review. Background Sickle cell disease is a serious inherited blood disorder where the red blood cells, which carry oxygen around the body, develop abnormally. Normal red blood cells are flexible and discâ€shaped, but in sickle cell disease they can become rigid, crescent shaped and also stickier. This can lead to blockage of blood vessels, resulting in tissue and organ damage and episodes of severe pain. The abnormal blood cells are more fragile and break apart, which leads to a decreased number of red blood cells, known as anaemia. Sickled red blood cells can block flow in blood vessels in the brain, leading to strokes. Strokes occur in up to 10% of children with sickle cell anaemia (HbSS) and can

cause limb weakness, slurred speech, seizures, and cognitive impairment. Two tests have been used in trials to identify children at higher risk of having a first stroke. One (transcranial Doppler ultrasonography) measures the speed of blood flowing through arteries in the brain, and those children with high blood flow are at increased risk of a stroke. The other (magnetic resonance imaging) takes images of the brain to see if there are any small areas of damage (silent strokes), those children with evidence of damage are at increased risk of stroke. Blood transfusions may help prevent a stroke by reducing the level of anaemia, diluting the sickled red blood cells, and increasing the level of oxygen in the blood. Blood transfusions can be linked to adverse events, e.g. the development of antibodies to proteins on donor red blood cells (alloimmunisation), accumulation of too much iron in the body from repeated transfusions, increased risk of infection, and extended length of stay in hospital. Search date The evidence is current to: 8 October 2019. Study characteristics We found five randomised controlled trials which enrolled a total of 660 participants. Three trials compared blood transfusions to no blood transfusions and two trials compared blood transfusion to the drug hydroxyurea. Trials were published between 1998 and 2016 and included children and sometimes adolescents; the majority had one form of sickle cell disease (HbSS). All trials received government funding. Key Results In children who are at a higher risk of having a stroke who have not had previous blood transfusions, a longâ€term blood transfusion regime probably reduces clinical strokes, and may also reduce other sickle cell diseaseâ€related complications.

48. Splenomegaly in the tropics.

1969

British medical journal

Marsden, P D and Hamilton, P J

49. A century after discovery of sickle cell disease: Keeping hope alive!

2014

Indian Journal of Medical Research

Mohanty, D

CASE REPORT

1. **A genetic study of six typical families of the sickle cell disease in India.**

   2010

   Child health and human development yearbook, 2010.

   Balgir, Ranbir S and RS, Balgir and Balgir, Ranbir S

The sickle cell disease is a genetically inherited hematological disorder commonly encountered in the Central-Southern region of India. It causes high degree of morbidity, mortality and fetal wastage in the underprivileged and vulnerable people. The gene frequency of sickle cell allele has been reported to be 4.3% in India. There is a dearth of typical phenotypic studies in India on the heterosis, mode of inheritance, clinical manifestations and hematological profile of various sickle cell disorders encountered in the affected families. This study highlights the genetic inheritance in six typical families of sickle cell disease with varied sickle cell phenotypes prevalent in the Central-Eastern region of India. Some intervention and prevention aspects of the different phenotypes of the sickle cell disease have been discussed for amelioration in the affected families and communities in the state of Orissa, India. (PsycInfo Database Record (c) 2021 APA, all rights reserved)

2. **Setting up and sustaining blood and marrow transplant services for children in middle-income economies: an experience-driven position paper on behalf of the EBMT PDWP**

   2021

   Bone Marrow Transplantation

   Faulkner, Lawrence and Verna, Marta and Attilio, Rovelli and Agarwal, Rajat Kumar and Rakesh, Dhanya and Lalith, Parmar and Amit, Sedai and Ankita, Kumari and Stalin, Ramprakash and Raghuram, C P and Pallavi, Mehta and Sandeep, Elizabeth and Sadaf, Khalid and Aliya, Batool and Khan, Ghilani Sarah and Itrat, Fatima and Tatheer, Zara and Priya, Marwah and Rajpreet, Soni and Deepa, Trivedi and Valentino, Conter and Canesi, Marta and Dosti, Othman and Vian, Faeq and Katharina, Kleinschmidt and Akif, Yesillipek and Lam, Catherine G and Howard, Scott C and Selim, Corbacioglu and Jefri, Abdulah Al and Alice, Bertania and Jochen, BÃ¼chner and AndrÃ¨, Willasch and Gibson, Brenda and Tayfun, GÃ¼ngÃ¼r and Marianne, Ifversen and Meisel, Roland and Ingo, MÃ¼ller and Kim, Vetteranta and Veys, Paul and Jacek, Wachowiak and Rovelli, A and Agarwal, Rajat Kumar and Dhanya, R and Parmar, L and Sedai, A and Kumari, A and Ramprakash, S and Raghuram, C P and Mehta, P and Elizabeth, S and Khalid, S and Batool, A and Ghilani, S K and Fatima, I and Zara, T and Marwah, P and Soni, R and Trivedi, D and Conter, V and Canesi, Marta and Othman, D and Faeq, V and Kleinschmidt, K and Yesillipek, A and Lam, Catherine G and Howard, Scott C and Corbacioglu, S and Jefri, Abdulah Al and Bertania, A and BÃ¼chner, J and Willasch, A and Gibson, Brenda and GÃ¼ngÃ¼r, T and Ifversen, M and Meisel, Roland and MÃ¼ller, I and Vetteranta, K and Veys, Paul and Wachowiak, J and Attilio, Rovelli and Agarwal, Rajat Kumar and Rakesh, Dhanya and Lalith, Parmar and Amit, Sedai and Ankita, Kumari and Stalin, Ramprakash and Raghuram, C P and Pallavi, Mehta and Sandeep, Elizabeth and Sadaf, Khalid and Aliya, Batool and Khan, Ghilani Sarah and Itrat, Fatima and Tatheer, Zara and Priya, Marwah and Rajpreet, Soni and Deepa, Trivedi and Valentino, Conter and Canesi, Marta and Dosti, Othman and Vian, Faeq and Katharina, Kleinschmidt and Akif, Yesillipek and Lam, Catherine G and Howard, Scott C and Selim, Corbacioglu and Jefri, Abdulah Al and Alice, Bertania and Jochen, BÃ¼chner and AndrÃ¨, Willasch and Gibson, Brenda and Tayfun, GÃ¼ngÃ¼r and Marianne, Ifversen and Meisel, Roland and Ingo, MÃ¼ller and Kim, Vetteranta and Veys, Paul and Jacek, Wachowiak

Severe blood disorders and cancer are the leading cause of death and disability from noncommunicable diseases in the global pediatric population and a major financial burden. The most frequent of these conditions, namely sickle cell disease and severe thalassemia, are highly curable by blood or bone marrow transplantation (BMT) which can restore a normal health-related quality of life and be cost-effective. This position paper summarizes critical issues in extending global access to BMT based on ground experience in the start-up of several BMT units in middle-income countries (MICs) across South-East Asia and the Middle East where close to 700 allogeneic

BMTs have been performed over a 10-year period. Basic requirements in terms of support systems, equipment, and consumables are summarized keeping in mind WHOâ€™s model essential lists and recommendations. BMT unit setup and maintenance costs are summarized as well as those per transplant. Low-risk BMT is feasible and safe in MICs with outcomes comparable to high-income countries but at a fraction of the cost. This report might be of assistance to health care institutions in MICs interested in developing hematopoietic stem cell transplantation services and strengthening context appropriate tertiary care and higher medical education.

3. **Phytomedicines (medicines derived from plants) for sickle cell disease.**

   2010

   The Cochrane database of systematic reviews

   Oniyangi, Oluseyi and Cohall, Damian H

BACKGROUND: Sickle cell disease, a common recessively inherited haemoglobin disorder, affects people from sub-Saharan Africa, the Middle East, Mediterranean basin, Indian subcontinent, Caribbean and South America. It is associated with complications and a reduced life expectancy. Phytomedicines (medicine derived from plants in their original state) encompass many of the plant remedies from traditional healers which the populations most affected would encounter. Laboratory research and limited clinical trials have suggested positive effects of phytomedicines both in vivo and in vitro. However, there has been little systematic appraisal of their benefits. This is an updated version of a previously published Cochrane Review. OBJECTIVES: To assess the benefits and risks of phytomedicines in people with sickle cell disease of all types, of any age, in any setting. SEARCH METHODS: We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register, the International StandardÂ Randomised Controlled Trial NumberÂ Register (ISRCTN), the Allied and Complimentary Medicine Database (AMED), ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP). Dates of most recent searches: Cochrane Cystic Fibrosis and Genetic Disorders Haemoglobinopathies Trials Register: 17 March 2020; ISRCTN: 19 April 2020; AMED: 18 May 2020; ClinicalTrials.gov: 24 April 2020; and the WHO ICTRP: 27 July 2017. SELECTION CRITERIA: Randomised or quasi-randomised trials with participants of all ages with sickle cell disease, in all settings, comparing the administration of phytomedicines, by any mode to placebo or conventional treatment, including blood transfusion and hydroxyurea. DATA COLLECTION AND ANALYSIS: Both authors independently assessed trial quality and extracted data. MAIN RESULTS: Three trials (212 participants) of three phytomedicines: Niprisan(Â®) (also known as Nicosan(Â®)), Ciklavit(Â®) and a powdered extract of Pfaffia paniculata were included. The Phase IIB (pivotal) trial suggests that Niprisan(Â®) may be effective in reducing episodes of severe painful sickle cell disease crisis over a six-month period (low-quality evidence). It did not appear to affect the risk of severe complications or the level of anaemia (low-quality evidence). The single trial of Cajanus cajan (Ciklavit(Â®)) reported a possible benefit to individuals with painful crises, and a possible adverse effect (non-significant) on the level of anaemia (low-quality evidence). We are uncertain of the effect of Pfaffia paniculata on the laboratory parameters and symptoms of SCD (very low-quality of evidence). No adverse effects were reported with Niprisan(Â®) and Pfaffia paniculata (low- to very low-quality evidence). AUTHORS' CONCLUSIONS: While Niprisan(Â®) appeared to be safe and effective in reducing severe painful crises over a six-month follow-up period, further trials are required to assess its role in managing people with SCD and the results of its multicentre trials are awaited. Currently, no conclusions can be made regarding the efficacy of Ciklavit(Â®) and the powdered root extract of Pfaffia paniculata in managing SCD. Based on the published results for Niprisan(Â®) and in view of the limitations in data collection and analysis of the three trials, phytomedicines may have a potential beneficial effect in reducing painful crises in SCD. This needs to be further validated in future trials. More trials with improved study design and data collection are required on the safety and efficacy of phytomedicines used in managing SCD.

4. **Myelonecrosis: A Clinicopathological Study from a Tertiary Care Center in South India over a Twelve-Year Period**

   2014

   Bone Marrow Research

   Rekha, J S and Kar, Rakhee and Basu, Debdatta and Jinkala, Sree Rekha and Kar, Rakhee and Basu, Debdatta

Aims. To study the etiology, diagnostic features, and clinical significance of myelonecrosis. Methods. A retrospective review of all trephine biopsies done over 12 years (January 2000 to December 2012) in Department of pathology was done and all trephine biopsies showing MN were identified and studied. Results. Twenty-five cases accounting for 0.4% were identified. Fever and generalized weakness were the common presenting symptoms. Anemia was seen in all cases followed by thrombocytopaenia. Malignancy was the underlying cause in 64% of cases; hematolymphoid malignancy was seen in two-thirds and solid malignancies in one-third of the cases. Tuberculosis accounted for 16% of the cases and the etiology was unknown in 12%. Conclusions. The causes of MN are varied and hematological malignancy and solid malignancies are the most common causes. Presence of myelonecrosis is associated with a poor prognosis. Myelonecrosis may obscure the underlying disorder and hence a thorough search in the bone marrow biopsy itself with the help of immunohistochemistry may prove worthwhile in identifying the underlying disease.

5. **Estimation of malondialdehyde levels in serum and saliva of children affected with sickle cell anemia**

   2018

   Journal of the Indian Society of Pedodontics and Preventive Dentistry

   Baliga, Sudhindra and Chaudhary, Minal and Bhat, Sham and Bhansali, Pooja and Agrawal, Akshat and Gundawar, Satwik

Background: Sickle cell anemia (SCA) is an inherited disorder of hemoglobin synthesis characterized by deformed erythrocytes. Hemoglobin S present in sickle-shaped erythrocytes exhibits an enhanced rate of auto-oxidation compared with normal hemoglobin A. It produces more of reactive oxygen species (ROS) which promotes oxidatively stressed environment. ROS degrade the membranes of sickle cell erythrocytes composed of polyunsaturated lipids and form malondialdehyde (MDA) as a by-product. Aim: The aim of the study is to evaluate and compare the MDA levels of serum and saliva in SCA patients. Design: A total of 150 children aged 4â€“12 years were divided into two groups: Group A (n = 75) consisting of children suffering from SCA and Group B (n = 75) consisting of healthy children. Blood and saliva samples were collected aseptically from both the groups, and they were subjected to thiobarbituric acid assay. Absorbance was evaluated spectrophotometrically at 531 nm, and the values of concentration of MDA were derived. Results: The mean MDA levels in serum and saliva were 8.9825 Â± 1.04 and 0.5152 Â± 0.28, respectively, in Group A and they were found to be higher than mean MDA levels of serum (5.87 Â± 0.92) and saliva (0.2929 Â± 0.06) of Group B and the difference of their mean was found to be statistically significant. Conclusion: A significant correlation of the MDA was found in saliva and serum of the patients with SCA. This finding suggests that saliva can be effectively used as a noninvasive alternative for assessing the oxidative stress in patients with SCA.

6. **Red Cell Indices and Hemoglobin Profile of Newborn Babies with Both the Sickle Gene and Alpha Thalassaemia in Central India**

   2018

   Indian Journal of Hematology and Blood Transfusion

   Upadhye, Dipti and Jain, Dipty and Nadkarni, Anita and Ghosh, Kanjaksha and Colah, Roshan

This study evaluated the effect of alpha thalassemia on the red cell indices and hemoglobin profiles of normal, sickle heterozygous and sickle homozygous newborn babies in central India where the sickle gene is linked to the Arab-Indian haplotype. 265 newborn babies were analysed with complete blood count and hemoglobin analysis on high performance liquid chromatography (Variant Hb Testing System, BioRad Laboratories, Hercules, CA, USA) using the Î²-thal short program. The sickle genotypes was confirmed by DNA analysis. The two common alpha gene deletions (âˆ’â€‰Î±3.7 and âˆ’â€‰Î±4.2) were detected by multiplex PCR. Among the 102 normal, 106 sickle heterozygous and 57 sickle homozygous newborns, the prevalence of a single alpha gene deletion (âˆ’â€‰Î±/Î±Î±) was 28.3% and that of deletion of 2 alpha genes (âˆ’â€‰Î±/âˆ’â€‰Î±) was 21.5%. In all, 57 normal (55.9%), 35 (33.0%) sickle heterozygous and 41 (71.9%) sickle homozygous newborns had a normal Î± genotype while âˆ’â€‰Î±/âˆ’â€‰Î± was seen in 23 (22.5%) normal, 30 (28.3%) sickle heterozygous and 4 (7.0%) sickle homozygous newborns respectively. The presence of associated alpha thalassemia resulted in a reduction in the hemoglobin levels and red cell indices in normal, sickle heterozygous and sickle homozygous newborn babies, MCV and MCH being strong discriminators of alpha thalassemia with two alpha gene deletions in all the three groups. This study also helped us to know the variations in hematological parameters in normal, sickle heterozygous and sickle homozygous newborns with and without associated Î± thalassemia.

7. **Left ventricular function by echocardiogram in children with sickle cell anaemia in Mumbai, Western India.**

   2015

   Cardiology in the Young

   Tidake, Abhay and Gangurde, Pranil and Taksande, Anup and Mahajan, Ajay and Nathani, Pratap

Introduction Cardiovascular events and complications are the leading cause of mortality and morbidity in patients with sickle cell disease. Cardiac abnormalities occur frequently and at an early stage in sickle cell anaemia patients, despite being more evident in adulthood. Sickle cell anaemia patients are increasingly able to reach adulthood owing to improved healthcare, and may, therefore, suffer the consequences of chronic cardiac injury. Thus, the study of cardiac abnormalities is essential in children Objective The aim of this study was to determine the echocardiographic changes in left ventricular function in children suffering from sickle cell disease in Mumbai, Western India. Methods The study comprised of 48 cases of sickle cell anaemia and 30 non-anaemic controls with normal haemoglobin and electrophoresis pattern. M-mode, two-dimensional, and Doppler echocardiographic measurements of patients and controls were performed according to the criteria of the American Echocardiography Society. Results On Doppler study, the A wave height was increased and the E/A ratio was decreased, whereas the deceleration and isovolumetric relaxation times were prolonged, which is typically seen in slowed or impaired myocardial relaxation ($p<0.001$). Although chamber dilatations were present, echocardiographic parameters showed no statistically significant correlation with severity of anaemia and age among the sickle cell patients. Conclusions We conclude that the increased left ventricular stiffness, compared with controls, might be due to fibrosis related to ischaemia caused by SS disease in addition to wall hypertrophy.

8. **Role of Emergency Automated Red Cell Exchange in Sickle Cell Crisis: A Case Report**

   2020

   Clinical Medicine Insights: Case Reports

   Gupta, A and Chaudhary, K and Kaushik, R and Anubhav, Gupta and Kiran, Chaudhary and Rajnish, Kaushik

For many years main stay of treatment for sickle cell anaemia was transfusion therapy. But repeated transfusions put the patient at risk of iron overload. Automated red cell exchange is an evolving and newer technique which rapidly removes the sickle cells and has benefit in decreasing sickle cell load and related complications. Red cell exchange is a therapeutic procedure in which the patientâ€™s whole blood is processed centrifugally in cell

separator. Patientâ€™s red cells are separated from other blood components and removed and replaced with donor red cells and colloids. We report our first experience of automated red cell exchange in 24-year-old female diagnosed case of sickle cell anaemia presented to us with acute chest syndrome with septic shock. Red cell exchange was planned to tide over the acute sickle cell crisis and provide symptomatic improvement. We also highlight that compound heterozygous thalassaemia could be associated with sickle cell disease which could make the diagnosis difficult. New generation automated Apheresis equipmentâ€™s provides better monitoring of the procedure that can be useful in severely ill patients also.

9. **Association of inflammatory biomarker C-reactive protein, lipid peroxidation and antioxidant capacity marker with HbF level in sickle cell disease patients from Chattisgarh**

   2012

   Indian Journal of Clinical Biochemistry

   Bhagat, S and Patra, P K and Thakur, A S

This study was undertaken to determine the association of inflammatory biomarker, oxidative stress and antioxidant capacity marker with fetal haemoglobin (HbF) level among sickle cell trait and sickle cell disease (SCD) patients in Chattisgarh. The study group consisted of 51 SCD (SS) patients with painful episode, 49 SCD (SS) patients with steady state, 50 sickle cell trait (AS) and 50 controls. Malondialdehyde (MDA), CRP, total antioxidant power (FARP), total thiol and HbF levels were quantified. We found a significant positive ($p < 0.0001$) association between CRP and MDA levels and its inverse association with HbF level in SS patients. We also observed that antioxidant capacity had significantly positively ($p < 0.0001$) associated with HbF level. The protective effect of HbF was found, because the increase in HbF levels resulted in decrease in lipid peroxidation and inflammation in SCD patients. A decrease in the HbF level and its antioxidant capacity has been associated with the pathogenesis of SCD. These finding may explain the high level of HbF is ameliorating oxidative stress and inflammation in SCD patients. Â© 2012 Association of Clinical Biochemists of India.

10. **Clinical events in individuals with sickle cell disease at a single center in Nagpur, India: Is sickle cell phenotype in India truly milder?**

    2012

    American Journal of Hematology

    Jain, D and Arjunan, A and Krishnamurti, L

Background: The clinical manifestations of sickle cell disease (SCD) in India are considered to be milder, explained in part by the Arab-India haplotype and co-inheritance of alpha Thalassemia. There are however, few studies of clinical events in large cohorts of patients with well defined phenotype. Further, there are limited data on the differences in the SCD phenotype among tribal and non-tribal ethnic groups. Objectives: To describe the clinical events in a cohort of patients with SCD followed at a single center in Nagpur, Maharashstra in central India. Methods: Clinical events described amongst patients with SCD followed at the Government Medical College Nagpur, Maharashtra from Jan 2008-August 2011 were analyzed for this study. Results: There were 5016 visits and 988 hospitalizations for 943 patients belonging most commonly to Mahar, Nav Buddha and Kunbi non-tribal ethnic groups. The reported median monthly household income was between Rs.1000-5000 ($19-94) with the highest level of education completed reported as high school degree or lower in 74% of the parents. Median age of patients was 10 years (range 1-43 years) with a median age of diagnosis between 2-5 years. Median time since last contact with the center was 10 months. Hgb SS genotype was observed in 85% patients. Twelve percent of patients received pneumococcal vaccination and 16% received penicillin prophylaxis. Thirteen percent of the patients (124 individuals) are receiving hydroxyurea treatment. Fever and painful crisis were the two most common clinical events, (32 and 9.1 cases per 100 person-years, respectively) followed by severe anemia and splenic sequestration. Thirty-five individuals died (1.06 deaths per 100 person-years; median age 7 years), 8 of infection, 7 of severe anemia, 4 of splenic sequestration, 2 during vaso-occlusive crisis and 1 of stroke. Ten

individuals died at home of unknown causes. Conclusion: In this large cohort of SCD patients drawn predominantly from non-tribal ethnic groups and followed at a single center, morbidity due to pain crises and infection and premature mortality were observed at a rate similar to that reported in the cooperative study of sickle cell disease (Vichinksy et al 1995). The high prevalence of severe anemia is intriguing for the possibility of interaction of SCD with malnutrition. The high rate of deaths at home point to systemic barriers to health care access. These data suggest the need for further studies of the clinical phenotype and the interaction of genetic and environmental factors in determining SCD phenotype in various ethnic groups in India.

11. **Diagnosis of a novel hemoglobinopathy of compound heterozygosity of hemoglobin S/hemoglobin Q India**

    2015

    Clinica Chimica Acta

Background: A novel double heterozygosity for the Î± chain variant Hb Q India and Î² chain variant Hb S is described. Hb S is prevalent in the central part of India while Hb Q India in its heterozygous state is found mainly in Sindhi families. Methods: Identification of both the variants, Hb S and Hb Q India, was done based on chromatograms of HPLC and capillary zone electrophoresis (CE). Confirmation of variants was done by PCR based amplification refractory mutation system (ARMS) technique. Results: Both HPLC and CE confirmed the presence of Hb S. HPLC showed a pointed narrow peak of Hb Q India at retention time of 4.55. min while it is eluted in Hb D zone on CE. A hybrid variant of these Î± and Î² globin chains was eluted in Hb C window and Hb C zone on HPLC and CE respectively. Molecular studies using ARMS technique confirmed these findings. Both the cases showed positive sickling test and presented with mild anemia. Conclusion: This is a unique 2 index cases for compound heterozygosity of Hb S with Hb Q India.

12. **Pentazocine dependence in sickle cell anaemia: A case report**

    2015

    Indian Journal of Psychiatry

    Gupta, P and Dayal, P

Introduction: Sickle cell anaemia is a chronic condition characterized by recurrent episodes of acute severe painful crises. Injectable opioids are the mainstay of management of painful crises. Little clarity exists regarding role of sickle cell anaemia in the onset of substance dependence. Aim: To demonstrate pentazocine dependence in a patient with sickle cell anaemia. Methodology: Detailed clinical interview in a specialist de-addiction centre (NDDTC). Results: A 29 year old male diagnosed with sickle cell anaemia in early childhood, had recurrent painful vaso-occlusive crises requiring symptomatic in-patient management, including injectable opioids. Patient received injectable pentazocine during one such crisis at 16 years of age. Apart from pain relief, patient also experienced a high. With worsening of frequency of crises and financial problems associated with recurrent hospitalisations, patient tried self-medicating with pentazocine. Use continued due to pain relief and the feeling of well-being. Gradually, daily use of injections started even when the pain crises were resolved. Withdrawals, tolerance and craving appeared which were unrelated to pain symptoms. Outpatient detoxification was unsuccessful but patient remained abstinent from injections on oral dextropropoxyphene. He kept relapsing to previous pattern of pentazocine use with every sickle cell crisis. Patient had good psycho-social support and was motivated to quit. OST could not be provided due to logistic issues. Inpatient management was advised which the patient did not comply with. Discussion: Pseudoaddiction, i. e., pain related behaviours which resemble dependence, is often documented in sickle cell patients. Higher estimates of addiction in such patients are frequent which might lead to undertreatment. But actual prevalence is largely unknown. Our patient had diagnosable opioid dependence. Management of such patients pose a big challenge. Conclusion: More research is needed on the association of sickle cell anaemia with substance dependence and the management of this condition.

13. **Left ventricular myocardial performance assessed by 2-dimensional speckle tracking echocardiography in patients with sickle cell crisis.**

    2012

    Indian heart journal

    Sengupta, S P and Jaju, R and Nugurwar, A and Caracciolo, G and Sengupta, P P

The status of left ventricle in sickle cell anemia presenting in sickle crisis and follow up has been minimally studied in past. To determine the left ventricular (LV) myocardial performance in these patients, we performed the study to assess two dimensional strains imaging which allowed a rapid and an accurate analysis of global and regional LV myocardial performance in longitudinal, radial, and circumferential directions. In this prospective study, 2-dimensional echocardiography (2DE) images of the LV were obtained in 52 subjects which included 32 patients (23 Â± 8yrs, 16 male) with homozygous sickle cell anemia (SCA) in sickle cell crisis and 20 healthy controls (23 Â± 5 yrs, 11 male) using apical 4-chamber and parasternal short-axis at the basal, mid, and apical levels. Of these 32 patients, 2DE was performed again in 18 patients in follow up (8 months Â± 5 days). Longitudinal, circumferential and radial strains (LS, CS and RS respectively) were quantified and compared in an 18-segment model using a novel speckle tracking system (2D Cardiac Performance Analysis, TomTec Imaging System, Munich, Germany). There was no significant difference in LV ejection fraction between both the groups (59.32 Â± 12.6 vs. 52.3 Â± 7.9; p-value > 0.05). In comparison with normal controls and follow up of sickle cell patients, peak LS was significantly attenuated in the subendocardial and subepicardial regions during sickle cell crisis ($p < 0.05$). However, a significant reduction in circumferential strain was evident only in subepicardial region ($p < 0.001$). Also patients in sickle cell crisis showed significantly higher radial strain parameters than controls ($p < 0.001$). Patients with SCA presenting in sickle cell crisis have reduced longitudinal shortening. LV myocardial performance remains unaltered due to relatively preserved circumferential shortening and increased radial thickening.

14. **Epidemeological profile of sickle cell disease prevalent in Chhattisgarh, Central India**

    2013

    International Journal of Pharma and Bio Sciences

    Patra, P K and Panigrahi, S K and Banerjee, G

330 clinically suspected sickle cell disease (SCD) patients admitted to Dept. of Pediatrics, Medical College & Hospital, Raipur (Chhattisgarh) between 9 months to 14 years of age within the time period of May 2000 to September 2007 were chosen as subjects for this study. The diagnosis of SCD was confirmed by Sodium Metabisulphite method. On the basis of the results of electrophoresis the subjects were divided into two groups' i.e. Sickle Cell Anaemia (SCA) consisting of 195 patients and Sickle cell Trait (SCT) consisting of 135 patients. Detailed clinical examination, complete blood count, peripheral blood smear, bilirubin estimation, USG whole abdomen & digital radiograms of skull &limbs were done for every subject. Weakness is the commonest symptom followed by bone pain, abdominal pain, jaundice & fever respectively in decreasing order of prevalence. Pallor is the commonest sign followed by splenomegaly, lymphadenopathy, hepatomegaly & icterus respectively in the study population. When compared with incidences of clinical features &complications of SCD obtained from the studies on people of other parts of Indian sickle cell belt central Indian SCA are having worst features.

15. **Systemic lupus erythematosus mimicking vaso-occlusive crisis in sickle cell disease: A case report**

    2020

    Indian Journal of Hematology and Blood Transfusion

    Mohanty, R and Thakur, A

Aims & Objectives: Sickle cell anaemia is one of the most prevalent genetic disorder. It is rarely associated with connective tissue disorders. Sickle cell disease patients often present with multiple joint pain and arthralgia attributed to vaso-occlusion. These symptoms are similar to those of patients with connective tissue disorder. This often results in delay in diagnosis of the connective tissue disorder associated with sickle cell disease. Herein, we report a case of 20 year-old female with known sickle cell disease who was later diagnosed to also have associated systemic lupus erythematosus. Patients/Materials & Methods: PATIENT- A 20 year-old female patient admitted to department of general medicine, VIMSAR, Burla. MATERIALS and METHODS. Place of study - VSS institute of medical science and research sickle cell disease was established by sickling slide test and haemoglobin electrophoresis. Systemic lupus erythematosus was established fulfilling the ACR/EULAR criteria. Results: ANA and anti DsDNA titres were positive for systemic lupus erythematosus. Sickling slide test and Haemoglobin electrophoresis revealed sickle cell disease. She was then diagnosed as case osf systemic lupus erythematosus with sickle cell disease. After establishing systemic lupus erythematosus in known patient of sickle cell disease, she was started on steroids and hydroxychloroquine. Her symptoms improved and both her disease were under control. Discussion & Conclusion: DISCUSSION: In this case report we described a 20 year old female with coexistant systemic lupus erythematosus along with sickle cell disease. Systemic lupus erythematosus being a great imitator has a variety of clinical manifestations. Due to limited number of case reports of associated lupus erythematosus in patients with sickle cell disease the diagnosis of systemic lupus erythematosus is usually missed. Such patients usually lack skin manifestations as previously reported but usually had articular manifestations attributed wrongly to sickle cell crisis. Further the diagnosis of systemic lupus erythematosus had been established several years after the diagnosis of sickle cell disease was made owing to overlap of clinical features. CONCLUSION: This report illustrates the importance of searching for other associated diseases when a patient of sickle cell disease who is on appropriate therapy presents multiple times with the same complaints. Early initiation of appropriate treatment in these patients may decrease morbidity, mortality and improve the condition of living.

16. Frequency of alpha gene number and HMOX1 polymorphism in Indian sickle cell disease patients

2019

Indian Journal of Hematology and Blood Transfusion

Pandey, H and Ranjan, R and Singh, K and Sharma, A and Kishor, K and Mahapatra, M and Saxena, R

Aims & Objectives: The aim of the study was to correlate the effect of different genotypic factors with the sickle cell patient's phenotype. To determine the molecular and hematological correlation under influence of inherited co-factors like a deletion and Hmox1 polymorphism. Patients/Materials & Methods: A total 60 patients, presence of HbS were studied. Their clinical details, hemogram and HPLC findings were noted. GAP PCR was done for detection alpha deletion. Where as allele specific PCR was done for HMOX1 polymorphism. Results: A total of 60 sickle cell anemia patient's blood sample collected and characterized. After identification of mutation, subjects were categorized in three groups according to the presence of alpha thalassemia genotype. Eighteen patient had alpha deletions with a mean age 10.4 Â± 6.7 (10 male and 8 female) and 3 patient had anti Î±- 3.7 kb (alpha triplication) with mean age group 18 Â± 6.08 (2 male and 1 female) while 39 patients were without any alpha deletions with mean age of 11.41 Â± 8.07 (24 male and 16 female). Patient with presence of alpha deletions had higher hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) levels and mean corpuscular hemoglobin concentration (MCHC). Mean difference of hematological variables amongst patient with alpha deletions and without alpha deletions were statistically significant (p value<0.05). Highest frequency of alpha 3.7 heterozygous (50%), followed by alpha 3.7 homozygous (38.89%) and 4.2 heterozygous (11.11%) were found in sickle cell anemia patients. We report the higher frequency of splenomegaly (19.04%), acute chest pain (16.66%) and painful crisis (21.42%) in SCD patients without presence of alpha deletions while SCD patients with coexistence of alpha thalassemia had less frequency of splenomegaly, chest pain and painful crisis. Out of 60, 27 were heterozygous (AT), 19 were homozygous (TT) and 14 were normal (AA) genotype for HMOX1 polymorphism. Haematological parameters i.e. Reticulocytes, haemoglobin and red cell indices were improved in

HMOX1 (TT) carrier. The frequency of clinical condition was severe in Hmox1 heterozygous phenotype in sickle homozygous patients. Discussion & Conclusion: Discussion: The prevalence of splenomegaly is higher but leg ulcer, acute chest syndrome, priapism is lower than the west. This may be due to higher prevalence of alpha and beta gene co-inheritance with HbS in India than in the West. Conclusion: This study indicates that in sickle cell disorders, Î±-thalassemia co-existence ameliorates the phenotype and may play pivotal role in understanding the clinicopathological profile of these cases.

17. **Unusual stability exhibited by (AT)XN12(AT)Y motif associated with high fetal hemoglobin levels**

    2019

    Journal of Biomolecular Structure and Dynamics

    Roy, K and Mahendru, S and Kukreti, R and Kukreti, S

Quasi-palindromic sequences (AT)XN12(AT)Y present in HS2 (hypersensitive site 2) of the human Î²-globin locus are known to be significantly associated with increased fetal hemoglobin (HbF) levels. High HbF levels in some adults arise due to pathological conditions such as sickle cell disease and Î²-thalassemia. However, elevated levels of HbF are also associated with a reducing morbidity and mortality in patients with Î²-thalassemia and thus ameliorate the severity of the disease. Using gel-electrophoresis, ultraviolet (UV)-thermal denaturation, and circular dichroism (CD) techniques, we demonstrated that it exhibits a hairpin-duplex equilibrium. Intramolecular species (hairpin) were observed in both low and high salt concentrations in gel assay studies displaying the unusual stability of intramolecular species even at the high counter-ion concentration. The unusual stability of hairpin secondary structures was also demonstrated by the monophasic nature of the melting profiles for the oligonucleotides which persisted at low as well as high salt and oligomer concentrations. Change in CD spectra as a function of oligomer concentration indicates that the bimolecular duplex formation is selectively favored over monomolecular hairpin formation at and above 9 ÂµM oligomer concentration. Thus, we hypothesize that imperfect inverted repeat sequence (AT)XN12(AT)Y of HS2 of Î²-globin gene LCR forms the unusually stable hairpins which may result in the formation of a cruciform structure that may be recruited for binding by various nuclear proteins that could result in elevated HbF levels. Communicated by Ramaswamy H. Sarma.

18. **Genetic modifiers and severity of sickle cell anemia**

    2018

    International Journal of Laboratory Hematology

    Adekile, A

Sickle cell disease (SCD) is an autosomal recessive disease in which homozygotes (SS) have sickle cell anemia while other genotypes e.g. SÎ²-thal, SC, SD are compound heterozygotes. The phenotype is characterized by chronic hemolytic anemia, recurrent vaso-occlusion and vasculopathy. Irrespective of the Hb genotype, the hallmark of SCD is phenotypic variability, driven by genetic and environmental factors. The most recognized genetic modifiers are the Î²S-globin gene haplotype, HbF level and co-existent Î±-thalassemia trait. The haplotype that is associated with the mildest phenotype is the Arab-India haplotype that is characterized by a high level of HbF, which is modulated by cis-acting and trans-acting elements. The former resides primarily in the Xmn-1 C/T restriction site (rs7482144) polymorphism in the 5' HBG2 gene on chromosome 11, while the latter include QTLs in the oncogene, BCL11A on chromosome 2 and the HBS1L-MYB intergenic region on chromosome 6. Other modulators of SCD sub-phenotypes include the UGT1A1 (UDPglucuronyltransferase) polymorphism, which predisposes to hyperbiliribinemia and gallstones. SNPs in other inflammatory genes and signaling pathways e.g. Annexin II, BMP6 (bone morphogenic protein), TGF-Î² (transforming growth factor) may influence the development of stroke, osteonecrosis, acute chest syndrome etc in SCD.

19. **A genetic study of six typical families of the sickle cell disease.**

2014

India: Health and human development aspects.

Balgir, Ranbir S

This reprinted article originally appeared in International Journal of Child Health and Human Development, Vol 3(1), Jan-Mar 2010, 139-150.. The following abstract of the original article appeared in (see record 2011-06892-014). The sickle cell disease is a generically inherited hematological disorder commonly encountered in the Central-Southern region of India. It causes high degree of morbidity, mortality and fetal wastage in the underprivileged and vulnerable people. The gene frequency of sickle cell allele has been reported to be 4.3% in India. There is a dearth of typical phenotypic studies in India on the heterosis, mode of inheritance, clinical manifestations and hematological profile of various sickle cell disorders encountered in the affected families. This study highlights the genetic inheritance in six typical families of sickle cell disease with varied sickle cell phenotypes prevalent in the Central-Eastern region of India. Some intervention and prevention aspects of the different phenotypes of the sickle cell disease have been discussed for amelioration in the affected families and communities in the state of Orissa, India. (PsycINFO Database Record (c) 2016 APA, all rights reserved)

20. **Level of nitric oxide and antioxidant vitamins in sickle cell anaemia patients**

2012

Indian Journal of Physiology and Pharmacology

Hundekar, P S and Suryakar, A N and Karnik, A C and Katkam, R V and Joshi, N G and Ghone, R A

Sickle cell anaemia (SCA) is characterized with severe anaemia and vasoocclussive episodes. Nitric Oxide (NO) a potential vasodilator, synthesized from various cells including endothelial cell. However SCA is associated with endothelial dysfunction, a measure cognitive factor for pulmonary hypertension (PH) and vasoocclussive crisis. The present study was attempted to evaluate level of serum NO and plasma antioxidant vitamins A, E and C in homozygous (n=30) and heterozygous (n=30) sickle cell patients and compared with age and sex matched healthy controls (n=30). We found, significantly (P<0.0001) elevated level of serum NO and significantly (P<0.0001) depleted antioxidant vitamins in homozygous and heterozygous sickle cell patients compared to healthy controls. Our study reveals that oxidative stress may be a responsible factor for the reduced bioavailability of NO which can impair the vasodilation in sickle cell patients.

21. **Influence of single nucleotide polymorphisms in the BCL11A gene on HBF levels and the clinical presentation of sickle cell disease in central India**

2013

Indian Journal of Hematology and Blood Transfusion

Upadhye, D and Jain, D and Nadkarni, A and Ghosh, K and Colah, R

Three SNPs in the BCL11A gene which may be responsible for variations in HbF levels and clinical severity in sickle cell disease were studied. Introduction: Sickle cell disease has an extremely variable clinical expression. High HbF levels are often associated with a milder clinical phenotype. Genetic variations at 3 loci, HBB cluster on chromosome 11, HBS1L-MYB on chromosome 6q and BCL11A on chromosome 2p influence HbF levels and disease severity in sickle cell disease (SCD). Xmn1 polymorphism (rs7482144) accounts for around 20 % of the variation in HbF levels. Previous studies in two independent SCD cohorts showed a strong association between variants in the BCL11A gene and HbF levels and the clinical severity. We undertook a preliminary study to evaluate the effect of three BCL11A polymorphisms on HbF levels and clinical severity in sickle cell disease.

Materials and Methods: 43 SCD patients were studied. HbF levels were measured by CE-HPLC. Three polymorphisms in the BCL11A gene: rs4671393, rs11886868 and rs7557939 were genotyped by DNA sequencing. Results: Patients with the mutant allele GG and the AG allele in the rs 4671393 SNP showed lower HbF levels (22.0 Â± 7.27 %) than the AA allele (28.8 %). The CC allele of the rs 11886868 SNP was associated with higher HbF levels (25.0 Â± 7.69 %), than the CT allele (21.0 Â± 7.98 %) and the TT allele (18.6 Â± 5.93 %). Cases with the GG allele of the rs7557939 also showed higher HbF (24.0 Â± 7.69 %) than the AG allele (21.0 Â± 7.06 %) and the AA allele (19.0 Â± 12.02 %). 60 % of the patients were classified as severe. The GG allele of the rs4671393 SNP was much higher in severe (84 %) vs. milder patients (41 %). Conclusion: Different alleles of the 3 SNPs in the BCL11A gene had variable HbF expression and the GG allele of the rs4671393 was more common in patients with severe disease.

22. **Serum copper in sickle cell disease**

    1981

    Indian Pediatrics

    Behera, S K and Satpathy, K N and Patnaik, B K

55 children with sickle cell disease (32 SS+23 AS) and 25 normal children (control cases) between the age of 8 months to 12 years were studied for serum copper values. The presence of fetal hemoglobin in sickle cell anemia (SS) cases varied from 2 to 12.2% and in sickle cell trait cases (AS) varied from 9.8 to 7.2%. The mean serum copper values in male and female children were 133.1Â±35.45 and 132.2Â±27.4 microgram percent in control cases, 135.7Â±24.8 and 135.2Â±33.6 microgram percent in AS cases, 196.6Â±57.8 and 160.8Â±39 microgram percent in SS cases, respectively. There was a regression of the copper values as age advanced. Higher copper values were obtained in SS cases. There was insignificant sex difference in serum copper values.

23. **Hemoglobin sickle D Punjab - A case report**

    2005

    Indian Journal of Human Genetics

    Mukherjee, M B and Surve, R R and Gangakhedkar, R R and Mohanty, D and Colah, R B

Compound heterozygosity for Î²S/Î²D results in a severe hemolytic anemia and a clinical syndrome similar to that of sickle cell disease. Here, we report a case of HbSD Punjab disease. A 10 year old female child residing at Nagpur, Maharashtra presented with severe hemolytic anemia, hepatosplenomegaly and occasional pains in bones and abdomen. Initially, she was thought to be a case of sickle cell anemia, however, with the help of HPLC and molecular analysis it was confirmed as HbSD Punjab disease.

24. **Phenotypic heterogeneity in homozygous sickle cell disease: Role of co-inherited alpha thalassaemia**

    2016

    Indian Journal of Hematology and Blood Transfusion

    Gopinath, S and Arun Kumar, A and Neelakandan, K and Easwari, S and Shaji, R V and Eunice, S

Introduction and Background: Homozygous HbS (SCD) shows significant difference in the phenotypes and the previous studies have shown that this is mostly due to co-inherited genetic factors that affect the levels of Î± and

Î³ globins. Differentiating SCD with sickle-b thalassemia based on HPLC values is difficult in Indian patients due to the inherently high HbF levels. Although mean corpuscular volume (MCV) is a useful differentiation parameter, the patients with SCD can also present with microcytosis due to iron deficiency and coexisting Î± thalassaemia. This study aims to assess the role of Î± thalassaemia in determining the phenotype of patients with SCD. Patient/ Material and Methods: Haemoglobin analysis was done using VARIANT II HPLC and Î²-globin gene mutations were detected by reverse dot blot or direct DNA sequencing. Characterization of the Î± globin gene deletions and their copy numbers were done by multiplex deletion PCR and gene dosage multiplex fluorescent PCR, respectively. Results: A total of 195 patients with homozygous HbS (SCD) diagnosed at the Department of Haematology, CMC, Vellore were included in the study. Their haematological parameters are tabulated below. The patients were categorised into two groups: MCV<75 fL and MCV>75 fL. In the patients with low MCV, 69 % of them had co-existing Î± thalassemia, and these patients had a milder phenotype with higher hemoglobin levels and RBC counts compared to the patients without Î± thalassaemia (who had the most severe phenotype) and those with MCV>75 fL. Conclusions: SCD can present with variable phenotypes. Low MCV observed in a large number of patients is due to co-inherited Î± thalassaemia and DNA analysis of Î± thalassaemia is helpful in the differential diagnosis of SCD and HbS-Î² thalassaemia. (Table Presented).

25. **Electrospray mass spectrometric characterization of hemoglobin Q (Hb Q-India) and a double mutant hemoglobin S/D in clinical samples**

    2008

    Clinical Biochemistry

    Mandal, A K and Bisht, S and Bhat, V S and Krishnaswamy, P R and Balaram, P

Objectives: The clinical analysis of hemoglobin by ion exchange chromatography can result in ambiguities in identification of the nature of the globin chain present in patient samples. LC/ESI-MS provides rapid and precise determination of globin chain masses. Design and methods: Hemolysate of hemoglobin Q-India and hemoglobin S/D/F have been analyzed using ESI-MS. Tandem-MS has been used to establish mutation in Î± chain of hemoglobin Q. Results: The identification of hemoglobin Q-India is readily achieved by LC/ESI-MS, which establishes the presence of a mutant Î± chain differing in mass from normal Î± chain by 22Â Da. The site of mutation has been identified by tandem-MS analysis of a tryptic fragment encompassing residues Î±V62-K90. LC/ESI-MS screening has also provide an example of simultaneous occurrence of mutant globin chains containing Î²6E â†' V (Hb S, sickle) and Î²121E â†' Q (Hb D) variant. Expression of Î³G globin chain is also demonstrated in this sample. Conclusions: The site of mutation in hemoglobin Q-India is identified as Î±64D â†' H which differs from mutations Î±74D â†' H in Hb Q-Thailand and Î±75D â†' H in Hb Q-Iran. Mass spectrometric analysis of hemoglobins from a patient and her parents suggests inheritance of mutant Î² globin genes from both parents. Â© 2007 The Canadian Society of Clinical Chemists.

26. **Concurrent Rheumatic Mitral Stenosis with Sickling Hemoglobinopathy**

    2017

    IHJ Cardiovascular Case Reports (CVCR)

    Vaideeswar, P and Singh, H and Singaravel, S

Rheumatic heart disease, particularly rheumatic mitral stenosis and hemoglobinopathies, especially HbS can pose a problem in pregnancy. Though both these conditions have a high incidence and considerable geographic overlap in India, very few studies have reported these diseases occurring concurrently. This is a report of concurrent recently diagnosed rheumatic mitral stenosis and undiagnosed sickling hemoglobinopathy in a post-partum woman.

27. **Clinical, hematological, molecular characterization and response to hydroxyurea treatment of symptomatic 17 HbSE cases in Eastern India: The largest series in world**

2014

Indian Journal of Human Genetics

Patel, S and Meher, S and Mohanty, P K and Dehury, S and Purohit, P and Dora, P and Das, K and Patel, D K

Background: Sickle cell Hemoglobinopathy is a major public health problem in our region. Literature shows HbSE cases are less symptomatic. A compound heterozygote state of 17 cases of HbSE, the largest number hitherto reported in our centre, most of them were severely symptomatic and they responded well to Hydroxyurea treatment. Aims and Objectives: Clinical, hematological and molecular study of HbSE cases & their response to low and fixed dose of Hydroxyurea (10 mg/kg/ day). Material and Methods: Detailed clinical data, Sickling test, alkaline electrophoresis, CBC, Biochemical examination, CE-HPLC, ARMS-PCR, haplotype analysis and Î±-thalassemia were done at Sickle Cell Clinic & Molecular Biology Laboratory, VSSMCH, Odisha. DNA sequencing was done . Hydroxyurea was administered at a low and fixed dose (10 mg/kg/day) based on frequency of painful crisis (VOC) and hospitalization and their response was studied. Results: Thirteen out of 17 cases were symptomatic with repeated VOC and hospitalization. Presented at an early age (10 yr) they had moderate anemia. MCV, MCH and MCHC were low. 87.5 % showed Southeast Asian haplotype for Hb E (- +). One was asymptomatic having Atypical haplotype (+- +) with Î±- 4.2 Î±/Î±Î± . Other one having Atypical haplotype (+-+-+) with Î±- 4.2Î±/Î±Î± was on HU from two year of age. 50% (6/12) cases had Î±- thalassemia (three each with Î±- 3.7 & Î±- 4.2 allele) in heterozygous state. Xmnl polymorphism (presence of 'T' allele) was found in 90.9 %. Conclusion: This is the first report of 17 cases of HbSE, the largest cohort studied ever. Majority are symptomatic with 100% response to HU treatment. Presented at early age. Other associated genetic factors may be responsible for their severe symptoms which needs further research. Finding of different compound heterozygote SCD with symptoms may need consideration for Prenatal Diagnosis & pre-marital screening in our area.

28. **Allogeneic peripheral stem cell transplantation in sickle cell disease: single centre experience from north india**

2019

Pediatric Hematology Oncology Journal

Vohra, M B and Hamal, S and Chakraborty, S and VikasDua, M S

Objective: Sickle cell disease (SCD) is a haemoglobinopathy resulting from single nucleotide substitution in which valine replaces glutamine at sixth position of Î²-globin chain of haemoglobin A. It is characterised by production of HbS leading to anaemia, haemolysis, vaso-occlusive complications and multiorgan damage. Management of SCD is often challenging despite the availability of hydroxyurea and other supportive therapy. Allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative treatment available till date as gene therapy is still an experimental approach. However, HSCT is rarely performed in countries like India due to decreased awareness among people, limited resources, high cost and poor access to medical care. Design/Methods: Retrospective single centre study done in Bone marrow transplant unit of Fortis memorial research institute, Gurugram. All patients from 2014-2019 who underwent HSCT for SCD were included. Results: 22 patients of SCD with median age of 8.5 years (range 1â€“29 years) underwent allogeneic HSCT with M:F of 2.1:1.15 (68.2%) patients underwent matched sibling/related donor transplant whereas 7 (31.8%) underwent haploidentical transplant. Conditioning regimen used in matched donor transplant was Busulfan(12.8mg/kg)/Cyclophosphamide(120mg/kg)/horse Anti-thymocyte globulin(120mg/kg) with methotrexate and cyclosporine as graft versus host disease (GVHD) prophylaxis. 6/7 patients of haploidentical transplant were given 2 courses of pre-transplant immunosuppressive therapy (Fludarabine+Dexamethasone) followed by conditioning with Thymoglobulin(4.5mg/kg)/Fludarabine(210mg/m2)/Busulfan(12.8mg/kg) with post-transplant cyclophosphamide (100mg/kg), Mycophenolate mofetil (MMF) and tacrolimus as GVHD

prophylaxis. Remaining 1 patient received conditioning with Thymoglobulin (4.5mg/kg)/ Thiotepa (8mg/kg)/ Fludarabine (150mg/m2)/ Cyclophospahmide (29mg/kg)/ Total body irradiation (2Gy) with post-transplant cyclophosphamide (100mg/kg), MMF and tacrolimus as GVHD prophylaxis. Disease free survival was 93.3% (14/15 patients) and 85.7% (6/7 patients) in matched donor and haploidentical donor transplant respectively. One patient of haploidentical transplant had primary graft failure and1 patient of matched donor transplant died after 100 days because of bronchiolitis obliterans organizing pneumonia.Acute GVHD was seen in 6 (27.3%) patients and chronic GVHD occurred in 2 (9.1%) patients. Median time of follow up was 102 days (range 30 â€“ 814 days). Conclusion: SCD is a debilitating syndrome characterised by chronic anaemia, pain crises andmultiorgan damage leading to poor quality of life and significant reduction of life expectancy. Allogeneic HSCT offers disease free survival and improvement in quality of life in patients of SCD.

29. Structural variation within the beta-globin gene cluster among hbs haplotype groups

2018

Blood

Lurie, P and Tayo, B and Cooper, R S and Lettre, G and Wonkman, A and Ayodo, G and Obaro, S K and Akingbola, T S and Hanchard, N

BACKGROUND The severity of sickle cell anemia (SCA) has been associated with five specific haplotypes in the beta globin cluster, identifiable by distinct patterns of restriction fragment length polymorphism (RFLP). These RFLP-defined haplotypes, named according to the region where they were first discovered-Central Africa region (CAR), Benin, Senegal, Arabic-Indian, and Cameroon-suggested that the sickle cell mutation arose recently at least four independent times in Africa, each time on a different genetic background, and again in India-the Multi-centric Sickle Cell Model. The beta-globin locus, however, is prone to extensive structural rearrangements, and alongside observations of ancestral sequence haplotypes extending several hundreds of kilobases beyond the beta globin cluster, it has been suggested that there is more cis-variation in the beta-globin gene cluster than is evident from RFLP analyses, and current definitions of RFLP haplotypes may not accurately reflect the ancestral origin of the sickle mutation. This undescribed cis-variation is important to understanding inter-individual phenotype variation associated with the different haplotypes. To better define this variation, we have undertaken extended, long-range molecular haplotyping of the beta-globin cluster on differing RFLP haplotype backgrounds using real time single molecule sequencing (SMS). The SMS approach generates long, unbroken reads with uniform coverage, thereby allowing for detailed molecular phasing of RFLP haplotypes and identification of local structural variation that would otherwise be hidden within the complex repetitive elements of the beta-globin cluster. In so doing, we plan to evaluate the molecular evidence for a single origin for the sickle cell allele and identify potential cis-acting, disease-modifying, candidate variants within the beta globin cluster. METHODS DNA from 200 SCA patients from three countries in sub-Saharan Africa-Nigeria, Cameroon, and Kenya-were collected after informed consent. RFLP analysis revealed the majority of the patients to be homozygous for the Benin and CAR haplotypes, with a smaller sampling of Cameroon, Senegal, and Atypical haplotypes. From this group we selected 40 samples-representing the four main classical RFLP haplotypes in sub-Saharan Africa-were selected for SMS. PCR was used to tile barcoded amplicons across the cluster. SMS was performed on a Sequel machine (Pacific Biosciences). The resulting FASTQ sequences were de-multiplexed, read quality control filters were applied, and mapped to human reference genome Hg38, prior to annotation and calling of single nucleotide variants (SNV) and structural variants (SV). RESULTS Analyses have so far identified 227 insertions, 1 8 deletions, 7 duplications, 76 inversions and 1 3 translocations from long-read analyses of the initial 40 samples; the vast majority of these variants are not described in public variant databases. Atypical haplotypes demonstrated more translocation and duplication events than other haplotypes. Insertions ~48 kb upstream of the beta-globin locus control region and 1.3 kb upstream of G globin gene 2 (HBG2) were observed on 50% of Senegal and 45% of CAR haplotypes. Also, recurrent insertions ranging between 32bp and 1 length, 2.3 kb downstream of the beta globin gene (HBB), were seen on 50% of the Benin and 54% of the CAR haplotypes, but only once on S haplotypes. CONCLUSIONS Jump to Our findings suggest there are more cis-SVs within the beta-globin gene cluster than previously described. Work to validate these SVs using orthogonal methods and

complete similar analyses of SNVs is ongoing. Variation outside of the gene cluster will also be integrated with RFLP and within-cluster molecular haplotypes to investigate the ancestral origin of the mutation, and validated cis-acting variants will be used to identify markers associated with proxies of SCA disease modification

30. Pre-transplantation suppression of haemopoiesis is associated with a high rate of macrophage activation syndrome in PTCy haploidentical transplantation for haemoglobinopathies

2017

Blood

Katewa, S and Kharya, G and Karnik, L and Kassim, A A and De La Fuente, J

Post infusion of stem cell cyclosphosphamide (PTCy) has enable transplantation across the HLA barrier and with the use of reduced intensity conditioning protocols. This constitutes a very important development for conditions affecting populations poorly represented in the donor registries, like haemoglobinopathies. However, PTCy in haemoglobinopathies is associated with a high risk of primary graft failure using standard regimens unless additional interventions are applied: suppression of haemopoiesis pre-transplantation with hydroxycarbamide and azathioprine, and the addition of thiotepa. We report for the first time an unexpected high rate of macrophage activation syndrome with this approach. Three centres (two in India and one in London, UK) used a common protocol to undertake 87 haploidentical bone marrow transplants for patients with haemoglobinopathies. The backbone of the conditioning regimen was provided by the reduced intensity PTCy approach developed by John Hopkins University for haploidentical transplantation in SCD (BolaÃ±os-Meade, Blood 2012). This included the use of ATG 0.5 mg/kg day -9 and 2 mg/kg days -8 and -7 (total dose 4.5 mg/kg), fludarabine 30 mg/m2 days -6 to -2 (total dose 150 mg/m2), cyclophosphamide 14.5 mg/kg days -6 and -5 (total dose 29 mg/kg) and TBI 200 cGy days -1. Post-transplantation patients received two doses of cyclophosphamide 50 mg/kg on days +3 and +4 to delete alloreactive T cells whilst preserving haempoietic stem cells, and GvHD prophylaxis was provided from day +5 with MMF until day +35 and sirolimus targeting 10 - 15 ng/mL. The source of stem cells was bone marrow harvested following priming with filgrastim 10 mg/kg/day for five days and aiming to obtain a cell dose of >8 x 108 TNC/kg. Supportive care recommendations included granulocyte colony-stimulating factor commenced on day +7 and continued until neutrophils maintained independently >1 x 108/L. The additional components added to the backbone to reduce graft failure included strategies previously found effective in achieving such aim in transplantation for thalassaemia major: (1) suppression of the expanded endogenous haemopoiesis with hypertransfusions, hydroxycarbamide 30 mg/kg and azathioprine 3 mg/kg and for a minimum of 42 days pre-transplantation (Sodani, Blood 2004; Shen Eur Radiol 2008; Capelli, Br J Haematol. 2009) and (2) addition of thiotepa 10 mg/kg on day -7 to the conditioning regimen (Bernardo, Blood 2012). Eleven patients (12.6%) suffered from macrophage activation syndrome, resulting in death in seven of the patients. Six patients had sickle cell disease and five thalassaemia. Patients presented with persistent fever not responding to broad spectrum antibiotics and antifungals in 6 cases, unexplained cytopenias in three cases and both persistent fever and cytopenias in two cases. The majority of the patients developed haemophacytosis with cytopenias, elevated ferritin (median 54,200 mg/L, range 2,026 - 128,844), triglycerides (median 3 mmol/L, range 1.78 - 7.92) and all but two had organomegaly. The presence of rash was a rare feature, only found in two patients and fever was not found in three patients. HHV6 infection in the bone marrow was found in 6 patients in whom it was specifically looked for, the other five had concomitant infection with CMV in three patients, adenovirus in one patient and JC was found in a case presenting with ataxia. Those surviving presented later (median 80 days, range 22- 143 days) with preservation of the bone marrow cellularity (>50% with no further reduction) and responded to treatment with dexamethasone 10 mg/m2 and antivirals and had resolution within 50 days of presentation; whereas those who did not survive presented early (median 42 days, range 17 - 258 days) with a bone marrow cellularity <50% eventually leading to secondary graft failure (<5% of hematopoietic cells in the bone marrow), and only had a partial response to dexamethasone, antivirals and targeted monoclonal antibodies, which was not sustained. In conclusion, PTCy transplants for haemoglobinopathies receiving pre-transplantation strategies to reduce graft failure have a high risk of macrophage activation syndrome. This has not been previously recognized and has a high risk of death (two third of the cases) despite targetted treatment. We postulate that the pre-transplantation treatment allows alloreactive T cells escape the use of PTCy.

31. **Negative epistatic interaction of sickle cell trait and alpha-thalassemia against severe p. Falciparum malaria**

2014

Indian Journal of Human Genetics

Purohit, P and Patel, S and Dehury, S and Meher, S and Patel, K.D.D.K. and Mohanty, P K

Background: Malaria is the most important public health problem in India. Alpha-thalassemia and sickle cell trait hypothesized to protect against severity of P. falciparum malaria. Population based study showed the negative epistatic between these two inherited hemoglobin disorders. Aim and objective: To study the influence of alpha-thalassemia and sickle cell gene on the severity of P. falciparum malaria and its epistatic interaction when co-inherited together in the individual. Material and Methods: In this case-control study, 232 adult patients with P. falciparum malaria admitted in the Department of Medicine, were analyzed for sickle cell gene and alpha-thalassemia at Sickle Cell Clinic and Molecular Biology Laboratory, V.S.S. Medical College, Burla, Odisha. Age, gender and ethnic matched 232 individuals with no history of malaria since 5 years were taken as control. Sickle cell was confirmed by ARMS-PCR and alpha-thalassemia was analyzed by Multiplex-PCR. Results: Out of 232 patients, 184 were HbAA, 36 were HbAS and 12 were HbSS where as in control 198 were HbAA and 34 were HbAS. In both the patients and controls with HbAA, the incidence of alphathalassemia was 39.1% in patients compared to 51.0% in control (adjusted odd ratio [OR], 1.62; 95% CI, 1.08-2.43; p=0.023). Similarly the incidence of alpha-thalassemia was 22.2% in patients with HbAS compared to 52.9% in control with HbAS (adjusted [OR], 0.25; 95% CI, 0.09-0.71; p=0.012). The incidence of ARF, Jaundice, cerebral malaria and death were significantly lower in patients (HbAA) with alpha-thalassemia compared to patients (HbAA) without alpha-thalassemia. Patients co-inherited with both HbAS and alpha-thalassemia had a greater HbA/HbS ratio compared to patients with HbAS without alpha-thalassemia (p<0.01) leading to more clinical severity. Conclusion: Both sickle cell trait and alpha-thalassemia enjoy a selective advantage separately against P. falciparum malaria. These protective effects of both hemoglobin disorders become cancel when co-inherited together in the individual.

32. **Y-chromosome evidence of an African origin of Dravidian agriculture**

2010

International Journal of Genetics and Molecular Biology

Winters, C

Y-linked markers provide loci to investigate genetic connections between human populations that can offer abundant anthropological information. Ancestry informative markers for Dravidian speaking populations in India that cultivate African cultigens were analyzed. The frequency of shared Y-chromosomes and HLAs between Dravidian and African populations is consistent with a possible African origin for millet, the principal food staple of Dravidian speakers in India. The evolutionary and epidemiological implications of these findings are reported herein. Â© 2010 Academic Journals.

33. **Application of isotope exchange based mass spectrometry to understand the mechanism of inhibition of sickle hemoglobin polymerization upon oxygenation**

2017

Journal of Structural Biology

Das, R and Mitra, A and Bhat, V and Mandal, A K

Sickle hemoglobin (HbS) polymerization initiates in the deoxy state with the binding of hydrophobic patch formed by the isopropyl group of Î²Val6 residue of a hemoglobin tetramer with the hydrophobic pocket of another tetramer, whose hydrophobic patch binds to the hydrophobic groove of a third molecule. Subsequent elongation

of a single stranded polymer followed by the formation of a double strand and finally combination of seven such pairs of double strands results in a fourteen stranded fibrous polymer. Precipitation of this fiber inside the erythrocytes results in sickling of red blood cells. Surprisingly, the polymerization does not occur in the oxy state of HbS. Due to the unavailability of crystal structure of oxy form of HbS, the molecular basis of inhibition of polymerization in the oxy state is unknown to date. In the present study, we have attempted to understand the molecular mechanism of inhibition of polymerization by exploiting the exchange of backbone amide hydrogens of HbS with deuterated solvent. Hydrogen/deuterium exchange kinetics of peptide amide hydrogens of both oxy and deoxy form of HbS were monitored through ESI mass spectrometry. Upon oxygenation changes in the conformational flexibility across different regions of Î± and Î² globin chains in the tetrameric HbS molecule were investigated. It was observed that oxygenation led to perturbation in the conformation of several residues around the hydrophobic patch, groove of a tetramer and axial, lateral contacts across the double strands that are involved in HbS polymerization.

34. Pharmacological induction of foetal haemoglobin and its correlation with F-Cells in Severe HbE-Beta Thalassaemia

2016

Indian Journal of Hematology and Blood Transfusion

Biswas, S and Ray, R and Nag, A and Roy, K and Ghosh, K and Bhattacharyya, M

Introduction and Background: HbE-beta thalassemia is a common disorder in eastern India with varying clinical presentation. Pharmacological induction of foetal haemoglobin is shown to reduce disease severity in sickle cell disease. The efficacy of hydroxyurea in induction of foetal haemoglobin in severe HbE-beta thalassaemia and its correlation with F-cells was evaluated. Patient/Material and Methods: 60 patients with severe HbE-beta thalassaemia were started on Hydroxyurea (10 mg/kg/day). Their clinical and laboratory parameters were observed at the baseline level and every month during the follow-up period. All patients were followed up prospectively for transfusion requirement, drug effectiveness and toxicity. Their HbF was measured by HPLC and their number of F-cells was measured by Flow Cytometry. One normal adult and one cord-blood sample were used as control to detect the number of F-cells by Flow Cytometry. The mean proportion of F-cells in normal persons is 2.7 % Â± 1.4 %, with a range of 0.5 %-7.0 % (Blood. 1975 Nov; 46(5):671-682). Results: With median follow-up of 18 months, out of the 60 patients, 47 showed an increase in HbF level and their transfusion requirements reduced significantly. Their HbF level increased from 12.5 Â± 0.19 (mean Â± SD) to 30.5 Â± 0.21 (mean Â± SD), and maintained the same value with significantly reduced requirements of transfusion; proving the efficacy of the drug. The number of F-cells measured by Flow Cytometry was correlated with the HbF level by HPLC. It was observed in most cases the rise of HbF is associated with increase of F-cells, while in some the above pattern was not observed. The number of F-cells of a normal healthy adult was observed to be 0.8 % and the number of F-cells in cord blood was observed to be 92 %, which were taken as controls. Conclusions: Pharmacological induction of HbF lead to reduction of transfusion requirements in some patients with severe HbE-beta thalassaemia. By flow cytometry, the number of F-cells can be determined, which are actually responsible for the production of HbF (measured by HPLC). But it has been observed that rise of HbF is not always associated with proportionate increase of F-cells.

35. Detection of compound heterozygous sickle cell-Î²+ thalassaemia in a patient with extreme weakness, mild jaundice and moderate anaemia - A case report

2017

Journal of Clinical and Diagnostic Research

Chandra, S and Ali, M and Mishra, P and Kapoor, A K and Jindal, Y

A 16-year-old female complained of extreme weakness. She had moderate anaemia; her Haemoglobin (Hb) was 7.7 gm/dl. Peripheral blood smear showed few sickled red cells. Sickle cell test was positive. High-Performance Liquid Chromatography (HPLC) revealed elevated levels of HbS (38.4%) and HbF (15.7%). In addition, HbA2

concentration was 3.8% and HbA concentration was 42.1%. Results suggested a diagnosis of compound heterozygous sickle cell-Î²+thalassaemia. Sickle cell test was also positive with blood of patientâ€™s brother; Hb HPLC examination showed relatively low concentration of HbS (25.2%) suggesting a diagnosis of sickle cell trait. Chromatogram of patientâ€™s step sister suggested a diagnosis of thalassaemia trait. Findings of this study suggested that abnormal genes were inherited in the patient from both the parents. It was interpreted that repeated haemolysis in the patient might have contributed to anaemia, weakness, rise in indirect bilirubin and jaundice. Furthermore, high level of HbF (>12%) may interfere with polymerization of sickle haemoglobin suggesting beneficial effects of HbF-inducing agents which may inhibit sickling.

36. A novel Î² globin gene mutation in codon 7 produces a hemoglobin variant mimicking HbS in HPLC

2010

Indian Journal of Hematology and Blood Transfusion

Sathya, M and Edison, E S and Rajkumar, S V and Srivastava, A and Shaji, R V

Hemoglobin S (HbS) and b thalassaemia are highly prevalent haemoglobin disorders in the India. Laboratory diagnosis of these diseases is based on peripheral blood analysis and hemoglobin electrophoresis or cation exchange-high performance liquid chromatography that detects and quantitates different types of haemoglobins present in these patients. DNA analysis to detect molecular lesions present in the globin genes is required in where there is discordance of these results with the clinical phenotype. In this report, we describe a case of hypochromic microcytic anemia that had a novel hemoglobin variant that elutes in the S window in HPLC that could cause misdiagnosis without DNA analysis. The patient is a 6-year-old boy from West Bengal, referred to our department for the clinical evaluation for hepatosplenomegaly (liver 2 cm and spleen 1 cm). Hematological parameters were measured by an automated cell counter (LH 750, Beckman Coulter, USA). HbA, HbF and HbA2/E levels were obtained by CE-HPLC (VARIANT Bio-Rad, USA). DNA was extracted by standard protocol. Common Î² -thalassaemia mutations [Codon8/9(+G), Codon15 (Gâ†' A), IVS I-1(Gâ†' T), Codon30 (Gâ†'C), IVS I-5(Gâ†' C), IVS I-1(Gâ†' A), Codon41/42(-TCTT), Codon26 (Gâ†' A) (Î²E) and Codon6 (A?T) (Î² S)] were screened by reverse dot blot (RDB). Common alpha (a) globin deletions [-Î± 3.7, -Î±4.2, -SEA, -MED, -SA] were screened by multiplex PCR followed by agarose gel electrophoresis. DNA sequencing was performed using cycle sequencing kit on ABI 3130 Genetic Analyzer. The patient had a hemoglobin level of 11.4 g/dl with a MCV 55.6 fl. The sickling test showed that it is negative in both patient and mother. Hemoglobin electrophoresis in the patient and the mother detected an abnormal band at the position of HbS in both. Mother had additional HbA2 and HbA bands and patient had only HbA2. HPLC analysis confirmed the presence of a haemoglobin variant eluted in the S window of the chromatogram and this abnormal haemoglobin was in the levels of 82.4% in the patient and 37.9% in the mother, respectively. The HbF levels were slightly elevated in the patient (2.2%) while it was normal in the mother (0.8%). DNA analysis by reverse dot blot identified IVSI-5(Gâ†' C) in the patient while bS (Codon6 Aâ†'T) was not detected. DNA sequencing analysis revealed a novel missense mutation GAGâ†' CAG in the codon 7 position of the beta globin gene present in compound heterozygous with IVS I-5(G-C). This mutation causes a replacement of glutamate by glutamine which results in the formation of a haemoglobin variant. Twenty-eight such hemoglobin variants that elute at the position of HbS in HPLC have been described. This report describes a novel mutation in the beta globin gene which produces a haemoglobin variant that co-migrates or co-elutes with HbS in electrophoresis or HPLC. DNA analysis in this family helped us to avoid a misdiagnosis and the study illustrates a probable diagnostic pitfall using HPLC system for the diagnosis of sickle cell disease in Indian population.

37. Cerebral hemodynamics in children with sickle cell disease in india

2020

International Journal of Stroke

Gajjar, B and Sharma, A and Sharma, S and Sharma, V

Background and Aims: Sickle cell Disease (SCD) is a devastating childhood disease. SCD is an inherited blood condition seen most commonly among people of African, Arabian and Indian origin. Children with SCD(hemoglobin SSorHbSS) carry a significant stroke risk. Although,SCD in India is often considered to be

different than in other racial groups, the data on cerebral hemodynamic parameters and stroke related to Indian SCD are scarce Methods: In this ongoing study, we are including consecutive children with SCD aged 3-18 years in India. Data are recorded for age, gender, head circumference, hemoglobin level, Hemoglobin S level (HBS), history of blood transfusion and stroke during previous 2 years. Transcranial Doppler (TCD) evaluation of both middle cerebral arteries (MCA) is performed with Rimed DigiLite dual channel TCD system and SonaraTek. Time-averaged mean of the maximum (TAMM) velocities of for both MCAs is recorded. Results: The study has recruited 30 Children, 16(53.3%) of which are female. Mean age is 9 (SD 3) years. Average (SD) head circumference is 47(4) cm. All children have HBS>30%. Average (SD) peak systolic (PSV) and end-diastolic velocities (EDV) of MCAs are 91(18) cm/s and 41(6) cm/s, respectively. History of ischemic stroke or transient ischemic attack was noted in 3 (10%) participants). Majority (86%) of children had received blood transfusion (86%) and/or Iron chelating agent (90%) during previous 2years. TAMM >200cm/s, considered to be associated with high risk of stroke was noted in 6/30(20%) children, of which 5 were 2-8yrs of age. Conclusions: Cerebral hemodynamic abnormalities are common in Indian children with sickle cell disease. We anticipate to collect larger and reliable cerebral hemodynamic data for Indian SCD patients.

38. Prediction of physiological status of sickle cell anemic patients by quantitative observations of microscopic components of urine

2013

Trends in Medical Research

Wankhade, V and Andhale, R B and Lodha, S

In the present study, some cellular and crystalline components of urine of Sickle Cell Anemia (SCA) were studied. In total 67 samples were investigated. The normal and abnormal cellular components like presence of Red blood cells, White blood cells Epithelial cells, Renal tubules cells, Bacteria, Yeast and Protozoan were observed and counted. Noncellular components/crystals like Tyrosine, Cholesterol, A/T Phosphate, Leucine, B-Granule, Uric Acid, Oxalate and Cystine were counted. It was observed that RBCs, WBCs and Epithelial cells, Renal tubules cells, Bacteria, Yeast and Protozoan were in high number indicating various complications occurring in the body of sickle cell anemic patients. It was observed that RBCs were 13918.18/cummÂ±SE 4057.90 indicating tremendous hematourea, number of WBC were 224.59Â±50.002 SE, Sqaumous Epithelial cells were 35.68Â±10.989 SE, Renal cells were 110.68Â±74.15 SE. This indicates that SCA patients suffer from kidney damage, hematourea, Urinary Tract Inflammation, Interstitial nephritis, Glomerulonephritis and Pylonephritis. Â© 2013 Academic Journals Inc.

39. Sickle cell disorder-a family study with total ten children (8 homozygous and 2 heterozygous) from satpuda hilly ranges of Maharashtra

2014

Indian Journal of Human Genetics

Kulkarni, G T and Yeola, G H and Dalvi, P N and Prabhune, Y S and Patil, R V and Kate, S L and Manchanda, R

Sickle Cell Disorder is a common blood genetic disorder found among tribal population groups from Maharashtra State. Highest Prevalence (about 20%) have been reported among tribal population groups Madia, Gond Pardhan, Halba from Gadchiroli Dist. and Bhill & Pawara from Nandurbar District. Taking into consideration the need of tribal groups residing in the Satpuda hilly ranges of Nandurbar Dist. We established Community Control Program Centre with help of local tribal youths. The Centre is located between 3rd and 4th Hilly ranges of Satpuda at Roshmal Bk. Tal. Dhadgaon Dist. Nandurbar , Popularly known as Sickle Cell Dawakhana. The centre provides diagnositic facilities, Possible Treatment (Ayurvedic mostly), and counselling for last 16 years. We also conduct extended family studies of the index patient. While screening the families we came across one family wherein parents are Heterozygote's, having total ten children, 8 Homozygote's and 2 Heterozygote's. We collected all

information from the family and carried out haematological and other investigations. To our information, this is the first largest family report with 8 Homozygote children in world medical literature. We will present family pedigree analysis along with Haematological investigations.

40. **Francisella novicida Cas9 interrogates genomic DNA with very high specificity and can be used for mammalian genome editing**

    2019

    Proceedings of the National Academy of Sciences of the United States of America

    Acharya, S and Mishra, A and Paul, D and Ansari, A H and Azhar, M and Kumar, M and Rauthan, R and Sharma, N and Aich, M and Sinha, D and Sharma, S and Jain, S and Ray, A and Jain, S and Ramalingam, S and Maiti, S and Chakraborty, D

Genome editing using the CRISPR/Cas9 system has been used to make precise heritable changes in the DNA of organisms. Although the widely used Streptococcus pyogenes Cas9 (SpCas9) and its engineered variants have been efficiently harnessed for numerous gene-editing applications across different platforms, concerns remain regarding their putative off-targeting at multiple loci across the genome. Here we report that Francisella novicida Cas9 (FnCas9) shows a very high specificity of binding to its intended targets and negligible binding to off-target loci. The specificity is determined by its minimal binding affinity with DNA when mismatches to the target single-guide RNA (sgRNA) are present in the sgRNA:DNA heteroduplex. FnCas9 produces staggered cleavage, higher homology-directed repair rates, and very low nonspecific genome editing compared to SpCas9. We demonstrate FnCas9-mediated correction of the sickle cell mutation in patient-derived induced pluripotent stem cells and propose that it can be used for precise therapeutic genome editing for a wide variety of genetic disorders.

41. **Cutaneous Manifestations of Hydroxyurea Therapy in Childhood Case Report and Review**

    2004

    Pediatric Dermatology

    Issaivanan, M and Mitu, P S and Chakrabarti, M and Khairkar, P

Hydroxyurea is commonly used in the treatment of various myeloproliferative disorders. In conventional pediatric clinical practice, its use is limited to benign hematologic conditions such as sickle cell disease and thalassemia. Long-term hydroxyurea use is associated with various adverse mucocutaneous effects including hyperpigmentation, alopecia, leg ulcers, and lichenoid eruptions. We report a 10-year-old boy with chronic myelogenous leukemia who presented with hyperpigmentation of the skin and nails 3 months after the start of hydroxyurea therapy. Melanonychia of all 20 nails with involvement of all three mucocutaneous areas (skin, nails, and mucosa) at presentation was a unique feature in our patient. With the recently increasing pediatric use of hydroxyurea in a variety of disorders, its benign and not so uncommon cutaneous adverse effects are emphasized here.

42. **2D DIGE based proteomics study of erythrocyte cytosol in sickle cell disease: Altered proteostasis and oxidative stress**

    2013

    Proteomics

    Basu, A and Saha, S and Karmakar, S and Chakravarty, S and Banerjee, D and Dash, B P and Chakrabarti, A

Sickle cell disease (SCD) is a hemolytic disorder caused by a mutation in beta-globin gene and affects millions of people worldwide. Though clinical manifestations of the disease are quite heterogeneous, many of them occur

due to erythrocyte sickling at reduced oxygen concentration and vascular occlusion mediated via blood cell adhesion to the vessel wall. We have followed proteomic approach to resolve the differentially regulated proteins of erythrocyte cytosol. The deregulated proteins mainly fall in the group of chaperone proteins such as heat shock protein 70, alpha hemoglobin stabilizing protein, and redox regulators such as aldehyde dehydrogenase and peroxiredoxin-2 proteoforms. Proteasomal subunits are found to be upregulated and phospho-catalase level also got altered. Severe oxidative stress inside erythrocyte is evident from the ROS analysis and OxyblotTM experiments. Peroxiredoxin-2 shows significant dimerization in the SCD patients, a hallmark of oxidative stress inside erythrocytes. One interesting fact is that most of the differentially regulated proteins are also common for hemoglobinopathies such as EÎ² thalassemia. These could provide important clues in understanding the pathophysiology of SCD and lead us to better patient management in the future.Â© 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

43. Frequency distribution of the methylenetetrahydrofolate reductase polymorphisms in sickle cell hemoglobinopathy-A hospital based study in central India

2021

Clinical Epidemiology and Global Health

Patel, S and Nanda, R and Hussain, N and Mohapatra, E and Patra, P K

Background: Coexistence of polymorphisms of methylenetetrahydrofolate reductase (MTHFR) with sickle cell gene exerts synergistic effect on complications associated with sickle cell hemoglobinopathy. Therefore, the study was planned to determine the frequency distribution of the MTHFR C677T and A1298C genotypes in children diagnosed with sickle cell disease. Methods: A total of 249 children diagnosed with sickle cell anemia, between age group 5â€“18 years, were enrolled for the cross sectional study. The demographic and clinical details were entered in a structured questionnaire. Collected blood samples were analyzed for hemoglobin and DNA was extracted for genotypic assay for MTHFR C677T and A1298C single nucleotide polymorphisms (SNPs) by Real-time PCR. Results: The study groups comprised of 218 sickle cell trait (SCT) and 31 sickle cell disease (SCD) children. The caste distribution between the two study groups was quite uniform (X231 = 44.21, p = 0.06). Frequencies of homozygous mutants 677TT and 1298CC were 2% and 19.7% respectively. The odds for the variant forms for both SNPs were found to be greater in SCD group. The genotypic and allelic frequencies did not reveal any caste preponderance. The mean age (p = 0.001), weight (p < 0.001), height (p < 0.001), BMI (p < 0.001) and hemoglobin concentrations (p = 0.002) were lower in homozygous 1298CC but not so in 677TT children. A1298C also depicted significant association with BMI and anemia (p < 0.001). Conclusion: Homozygous mutant MTHFR variants would be essential genetic markers especially in children with SCD to identify the vulnerable group who frequently get hospitalized for vascular complications.

44. Induced expression of bone morphogenetic protein-6 and Smads signaling in human monocytes derived dendritic cells during sickle-cell pathology with orthopedic complications

2010

Biochemical and Biophysical Research Communications

Abhishek, K and Kumar, R and Arif, E and Patra, P K and Choudhary, S B and Sohail, M

BMP-SMAD (bone morphogenetic protein) signaling pathways in association with APT play paramount roles in osteoblastic differentiation, bone formation and embryonic development of human and animals. However, the implications of potent components (BMP6, Smad1, Smad2 and APT) of this pathway in SCD (sickle cell disease) pathology with orthopedic complications (Ortho + SS) are poorly elucidated and substantially unknown. Here, we address the role of BMP6, Smad1, Smad2 and APT mRNA and protein expression in hMDDCs obtained from Ortho + SS patients, employing RT-PCR, qRT-PCR and immunoblotting. Interestingly, we observed that SCD pathology exhibited significantly up-regulated expression of those signaling components at the level of mRNA and protein. Furthermore, exogenous BMP6 induced apoptosis was observed to be significantly associated in Ortho + SS complication and markedly increased the percentage of cells undergoing apoptosis as compared to

healthy group. Interestingly, the non-stimulated cells have shown higher apoptotic nuclei percentage than the stimulated cells in pathological condition. Thus, expression of BMP-SMAD signaling components augments apoptosis and up regulates the transcription of these genes and it suggests that induction is due to transcriptional regulation. Taken together, our findings provide evidence that BMP-SMAD signaling components along with APT were over expressed, mediates apoptosis and may play an important role in the SCD pathology with orthopedic complications. Â© 2010 Elsevier Inc. All rights reserved.

45. Sickle Cell Trait Presenting as Chronic Calcific Pancreatitis with Pseudocyst- A Case Report

2021

Indian Journal of Clinical Biochemistry

Shah, S and Jondhale, S and Nanda, R and Patel, S and Mohapatra, E and Goel, A K

Sickle cell disease is known to cause acute pancreatitis either due to gall stones obstructing the pancreatic duct or by vaso-occlusive mechanism. However chronic pancreatitis is a very rare complication in sickle cell anemia. We report a case of sickle cell trait presenting with chronic pancreatitis with pseudo cyst. USG abdomen and CT abdomen confirmed the diagnosis of chronic calcific pancreatitis with pseudocyst. Etiological work up for other causes did not reveal anything except sickle cell trait. This case represents a rare association between chronic calcific pancreatitis and sickle cell trait.

46. Modification of axial fiber contact residues impact sickle hemoglobin polymerization by perturbing a network of coupled interactions

2007

Protein Journal

Banerjee, S and Mirsamadi, N and Anantharaman, L and Sivaram, M V S and Gupta, R B and Choudhury, D and Roy, R P

The identity of intermolecular contact residues in sickle hemoglobin (HbS) fiber is largely known. However, our knowledge about combinatorial effects of two or more contact sites or the mechanistic basis of such effects is rather limited. Lys16, His20, and Glu23 of the Î±-chain occur in intra-double strand axial contacts in the sickle hemoglobin (HbS) fiber. Here we have constructed two novel double mutants, HbS (K16Q/E23Q) and (H20Q/E23Q), with a view to delineate cumulative impact of interactions emanating from the above contact sites. Far-UV and visible region CD spectra of the double mutants were similar to the native HbS indicating the presence of native-like secondary and tertiary structure in the mutants. The quaternary structures in both the mutants were also preserved as judged by the derivative UV spectra of liganded (oxy) and unliganded (deoxy) forms of the double mutants. However, the double mutants displayed interesting polymerization behavior. The polymerization behaviour of the double mutants was found to be non-additive of the individual single mutants. While HbS (H20Q/E23Q) showed inhibitory effect similar to that of HbS (E23Q), the intrinsic inhibitory propensity of the associated single mutants was totally quelled in HbS (K16Q/E23Q) double mutant. Molecular dynamics (MD) simulations studies of the isolated Î±-chains as well as a module of the fiber containing the double and associated single mutants suggested that these contact sites at the axial interface of the fiber impact HbS polymerization through a coupled interaction network. The overall results demonstrate a subtle role of dynamics and electrostatics in the polymer formation and provide insights about interaction-linkage in HbS fiber assembly. Â© 2007 Springer Science+Business Media, LLC.

47. Hemostasis in sickle cell disease

2020

Indian Journal of Forensic Medicine and Toxicology

Ibrahim, N K and Radhi, A and Al-Aubody, N M

Sickle cell disease results in a significant morbidity and mortality related to intra-vascular thrombosis. This study is an attempt to improve our understanding the role of hypercoagulability in the pathogenesis of sickle cell disease. A case group of 20 asymptomatic sickle cell adult patients in a steady-state were compared with a control group of 20 normal adult people, both groups aged (18-50) year and from both sex, to evaluate the process of hemostasis. An investigation has been done for both groups including estimation of hemoglobin, platelets count, bleeding time and clotting time. There is a highly significant increase in the number of platelets with ($P<0.01$) together with a highly significant decrease in bleeding time with ($P<0.01$) for a case group in comparison with a control group. There is no significant difference of clotting time between both groups. That may suggest that the platelets aggregation formation activity is significantly increase in patients with sickle cell disease in a steady-state.

48. Manipulation of developmental gamma-globin gene expression: An approach for healing hemoglobinopathies

2021

Molecular and Cellular Biology

Venkatesan, V and Srinivasan, S and Babu, P and Thangavel, S

Î²-Hemoglobinopathies are the most common monogenic disorders, and a century of research has provided us with a better understanding of the attributes of these diseases. Allogenic stem cell transplantation was the only potentially curative option available for these diseases until the discovery of gene therapy. The findings on the protective nature of fetal hemoglobin in sickle cell disease (SCD) and thalassemia patients carrying hereditary persistence of fetal hemoglobin (HPFH) mutations has given us the best evidence that the cure for Î²-hemoglobinopathies remains hidden in the hemoglobin locus. The detailed understanding of the developmental gene regulation of gamma-globin (Î³-globin) and the emergence of gene manipulation strategies offer us the opportunity for developing a Î³-globin gene-modified autologous stem cell transplantation therapy. In this review, we summarize different therapeutic strategies that reactivate fetal hemoglobin for the gene therapy of Î²-hemoglobinopathies.

49. Rare presentation and successful management of cerebral sinus venous thrombosis in a patient with sickle cell trait

2020

Journal of Clinical and Diagnostic Research

Khan, K and Chaturvedi, A

Cerebral Venous Thrombosis (CVT) is an uncommon cause of stroke and is generally present with headache. Due to its widely varying clinical features, risk factors, radiological findings, and outcomes, it is very difficult to diagnose it in initial stage. Early diagnosis of CVT and its treatment can reduce the disease progress, its burden and risk of acute and long-term complications including mortality. A 23-year-old male patient was admitted from casualty department with complaints of severe generalised headache and photophobia since one week and four episodes of Generalised Tonic Clonic Seizures (GTCS) with post-ictal confusion and drowsiness since two days. All investigations were insignificant for the cause except that he was a sickle cell trait (AS pattern), that lead to CVT related headache and convulsion. He was treated with hydration in the form of intravenous fluids, warfarin, mannitol and syrup glycerol, Tab. Sodium bicarbonate and Tab. Hydroxyurea.

50. An interesting case of compound heterozygous sickle cell-B+ thalassaemia presenting with acute chest syndrome

2010

Journal of Clinical and Diagnostic Research

Jailkhani, R and Patil, V S and Kulkarni, S P and Pervatikar, S and Jayashankara, B B

Sickle cell disease is a hereditary disorder which is caused due to a mutation in the Î²-globin gene. Acute chest syndrome is a rare complication which is seen in sickle cell patients in India. Here, we are presenting an interesting case of compound heterozygous Sickle cell-Î²+ thalassaemia who presented at the age of 20 years with acute chest syndrome and massive hepatomegaly. The patient also typically had veno-occlusive crisis. The diagnosis was based on the presence of numerous sickle cells in the peripheral smear and also on the presence of a strong HbS (68%) band on cellulose acetate electrophoresis supported by increased HbA2>3.5% and decreased cell indices. His mother was reported to have Sickle cell trait, who was asymptomatic with HbS(35.7%) and HbF (1.1%).

51. The hand-foot syndrome in sickle-cell haemoglobinopathy

1995

Journal of Bone and Joint Surgery - Series B

Babhulkar, S S and Pande, K and Babhulkar, S

The hand-foot syndrome is a benign self-limiting condition seen in young children with sickle-cell haemoglobinopathy, usually at the time of a crisis. The authors have observed 36 cases among 4920 patients. The features and management of the condition are discussed and the published literature is reviewed.

52. Hydroxyurea-induced azure lunula: Case Report

2021

Journal of Dermatology and Dermatologic Surgery

Chandak, S and Madke, B and Jawade, S and Singh, A

Alteration in the color of the lunula can either be due to a cutaneous or systemic disorder or may be due to a drug effect. Azure or blue lunula is a disorder of pigmentation of nail lunula. This bluish discoloration was noted in fingernails of both hands and great toes. Hereby, we report a case of azure lunula in a child with sickle cell disease receiving oral hydroxyurea 500 mg daily.

53. Sickle cell disease: Presenting as cirrhosis of liver

2020

Indian Journal of Hematology and Blood Transfusion

Beura, B P and Karua, P C

Aims & Objectives: Sickle Cell Disease- Presenting as Cirrhosis of Liver. Sickle cell disease is a common haemoglobinopathy which may present with multiple symptoms. The major features are related to haemolytic anemia and vasooclusion. We report a case of an undiagnosed sickle cell disease presenting with cirrhosis of liver. Patients/Materials & Methods: A 37 year non-alcoholic male presented with abdominal distension and yellowish discoloration of eyes and urine. On examination there was pallor,icterus and features of ascites. Laboratory investigations suggested severe anaemia, features of haemolytic jaundice, normal ferritin and elevated LDH. Peripheral blood smear showed sickle shaped RBCs and reticulocytosis. Haemoglobin electrophoresis showed 76.1% HbS. HBsAg and HCV RNA were negative. Coomb's tests were negative. Ultrasound abdomen showed hepatomegaly with coarse hepatic echotexture with dilated portal vein and sludge filled gall bladder and gross ascites. Ascitic fluid analysis showed SAAG of 1.5. Upper GI Endoscopy showed grade II esophageal varices. There was history of 1 unit blood transfusion 2 years back. Test with observed value and reference in the bracket Haemoglobin 5.6gm/dl (male 14-17 gm/dl) Reticulocyte count 10.5% (0.5-2.5%). Total bilirubin 10.4 mg/dl (0.2-1.2 mg/dl) Direct bilirubin 4.8 mg/dl (0-0.4 mg/dl SGOT 93 IU/L (0-40 IU/L) SGPT 59 IU/L (0-40 IU/L) ALP 115 IU/L (<250 IU/L) Serum Urea 26 mg/dl (10-40 mg/dl) Serum creatinine 1.2 mg/ dl(0.5-1.5 mg/dl) S.albumin 2.9 gm/dl (3.6-4.8 mg/dl) Ascitic fluid albumin 1.4 gm/dl PT/INR 1.63 (<1.5) S.LDH 760U/L (240-480 U/L)

S.Ferritin 54 ng/ml (20-250 ng/ml) G6PD 24.78U/g Hb (6.4-8.7 U/g Hb) Coombs test (direct & indirect) Negative HIV Negative HBsAg Negative HCV RNA Negative Haemoglobin electrophoresis HbS 76.1% HbF 18.3% HbA2 2.2% Ascitic fluid analysis Appearance clear Total cell count- 420/cmm(mostly lymphocytes) Sugar 88 mg/dl Albumin 1.4 mg/dl ADA 18 Gram staying No organism seen ZN stain AFB not detected Chest xray - Normal Results: The cirrhosis of Liver in our patient is due to sickle cell disease. Discussion & Conclusion: The heaptobiliary manifestations may vary from asymptomatic incidentally detected abnormal liver function tests to decompensated liver failure. It is important to recognise the rare presentations of the disease for better patient care.

54. Homozygous hemoglobin D with alpha thalassemia: Case report

2011

Open Journal of Hematology

Pandey, S and Mishra, R M and Pandey, S and Saxena, R

Hb D is a clinically silent condition, but co-inheritance of Hb D with sickle cell or thalassemia produces clinically significant conditions like sickle cell anemia or thalassemia intermedia and chronic hemolytic anemia of moderate severity. Here we present a case of homozygous Hb D with alpha 3.7kb deletion and phenotypic effect on patients. Diagnosis of Hb D patient was performed by high performance liquid chromatography (HPLC) and complete blood count was measured by automated cell analyzer. Molecular study for common alpha deletions done by Gap-PCR. A homozygous Hb D patient with alpha thalassemia was present mild clinical manifestations with normal reticulocytes and red cell indices. Thus observed case conclude the co-existence of alpha 3.7 deletions with homozygous Hb D present mild clinical -hematological picture. Â© Saxena et al.

55. Retrospective analysis of the hb a2 value in sickle cell positive population in Central Gujarat, India

2017

Blood

Bhatwadekar, S S and Shah, P and Shah, S and Toprani, H and Shah, B and Desai, D and Zanzarukiya, B B and Patel, T S and Toprani, T

Introduction: Sickle cell disease (SCD) is one of the commonest autosomal inherited diseases globally. India has high Sickle cell disease burden, presented with very wide clinical phenotypes. Gujarat state particularly central and south region of state has a high prevalence of the sickle cell anemia. Though being commonly encountered in this region, there are hardly few large scale studies done on sickle cell anemia and its clinical impact on health. With this background in mind, we did this retrospective analysis of laboratory parameters to understand the correlation of HbA2 values in sickle cell population. Materials and Methods: This retrospective analysis of Capillary electrophoresis (CE) or High performance liquid chromatography (HPLC) results of total 30845 sample size was done. Study period June 2013 to June 2017. Investigation carried out at 4 different laboratories was reviewed for analysis of Hemoglobin A2 (HbA2) values in Sickle cell population in the central Gujarat region of India. Hematological indices, Solubility tests, were also taken into considerations. Initially, all the data were reviewed and analyzed separately and then they were compiled together and analyzed. Out of 30845, 28495 results were reviewed. Rests were omitted either due to incomplete data. On capillary electrophoresis 19383 tests were conducted, whereas, 9112 tests were conducted on HPLC. Result Out of total 28495 samples, 2327 were sickle positive, 846 had HBS >50% (SCD), 1471 had HBS<50% Sickle cell trait (SCT), 26168 no sickle window. With respect to HbA2 value, we divided them further into 3 groups. Group 1 : HbA2 between 2-3.5%, Group 2 : HbA2 more than 3.5% and Group 3:HbA2 less than 2%. Further sub analysis of all the 3 groups was done on the basis of MCV. As we assume that high HbF with HbA2<2% may be associated with Î´-Î² thalassemias and low HbF with HBA2<2% may be associated with Î±-thalassemia, in group 3, Hb F was also considered in sub analysis. The results of the analysis are as depicted in table. Conclusion In this retrospective analytic study we found that SCD can be categorized into 3 groups based on HB A2 value, further sub analysis with respect to MCV and HB

F value shows, 644 (75.2%) have probability of having co inheritance of Thalassemia (MCV< 80 FL), remaining 212(24.8%)may be representing homozygous SCD with no co inheritance of Î± or Î² or Î´-Î² Thalassemia (MCV>80 FL).As we could not find single sample having HBA2 <2% with HBF(<10%) with low MCV in SCD category, raises possibility are we dealing with Î´-Î² Thalassemia in this study population? These patients require further family studies and molecular study to confirm co-association of Thalassemia.There is high possibility that heterogeneity in clinical presentation of SCD patients found in Gujarat may have correlation with low MCV and variability in A2 value (indirect evidence of underlying coinheritance of Thalassemia). Prospective large cohort study is required to document clinico-pathological correlation.

56. F-cell levels are altered with erythrocyte density in sickle cell disease

2011

Blood Cells, Molecules, and Diseases

Basu, S and Dash, B P and Patel, D K and Chakravarty, S and Chakravarty, A and Banerjee, D and Chakrabarti, A

Lighter cells from density fractionated erythrocytes of sickle cell disease (SCD) patients carry higher amount of externalized phosphatidylserine (PS) and cell surface glycophorins compared to the denser counterparts. Further analysis also revealed that the denser cells contained higher levels of fetal hemoglobin (HbF) compared to the lighter cells, supported by the presence of larger number of F-cells in these populations. In this report, we have found direct evidence on the higher survival of the HbF rich erythrocytes in SCD. Â© 2011 Elsevier Inc.

57. Unusual presentation of sickle cell anaemia - Paraplegia in a fifty year old man

2005

Indian Journal of Pathology and Microbiology

Yaranal, P J and Basu, D and Udaya Prashant, P and Dutta, T K

A fifty-year-old male patient presented with bilateral lower limb paraplegia. He was subsequently found to have sickle cell anaemia. The patient showed good response to treatment. Central nervous system complications in sickle cell anaemia are well known. However paraplegia has rarely been documented in sickling disorders. We report this case because of rarity of sickle cell anaemia presenting in old age with paraplegia.

58. VEGF Promoter Region 18-bp Insertion-Deletion Polymorphism in Sickle Cell Disease Patients with Microalbuminuria: A Pilot Study

2019

Indian Journal of Hematology and Blood Transfusion

Amle, D B and Patnayak, R L and Verma, V and Singh, G K and Jain, V and Khodiar, P K and Patra, P K

Purpose: Vascular endothelial growth factor (VEGF) is a potent inducer of micro vascular permeability thus leading to nephropathy. Insertion/deletion (I/D) polymorphism of 18Â bp at â^'Â 2549 position in VEGF gene causes increased transcription leading to increased production of VEGF. Thus, we aimed to associate I/D polymorphism of the 18Â bp fragment at â^'Â 2549 position of the promoter region of VEGF gene with sickle cell nephropathy (SCN). Methods: This observational analytical case control study included 30 subjects each of SCN, sickle cell disease (SCD) without nephropathy and the control group. The subjects were assessed for various hematological and biochemical parameters. Further, 18Â bp I/D polymorphism of VEGF gene in all three study groups was assessed by polymerase chain reaction followed by electrophoresis and compared. Result: Though increased frequency of both DD genotype and D allele was found in SCN compared to SCD and control, only

frequency of D allele was found to be significantly higher (p = 0.04). D allele posed marginal risk of microalbuminuria in SCD subjects compared to controls (OR = 2.11) as well as to SCD without MA subjects (OR = 1.84). Conclusion: D allele in I/D polymorphism in the promoter region of VEGF gene may be associated with marginal increase in risk of susceptibility to sickle cell nephropathy.

59. Concurrent presentation of sickle cell disease with acute promyelocytic leukemia: A rare case report

2013

Indian Journal of Hematology and Blood Transfusion

Chauhan, S and Das, P K

A 23 year old female presented with breathlessness for one month, diagnosed to be a case of Sickle cell disease, Bone marrow examination revealed APML. Introduction: Very few articles have highlighted the occurrence of Acute Leukemia after 10-15 years of treatment for Sickle cell disease as a consequence of Hydroxyurea. However no case has been reported in the literature of concurrent presentation of such two pathologies involving two Haematopoietic cell lineages. We report a highly rare case. Materials and Methods: CASE REPORT: A 23 years old female presented with breathlessness for last one month, low grade fever and whole body swelling for one week. By the time the patient came had received three units of Blood Transfusion O/E hepatomegaly, mild Splenomegaly. Routine hematological investigation revealed HB-8.2 g/%, TLC-680/mm3, TPC-68,000/mm3, DC-70 % neutrophil, HB electrophoresis revealed Hbs. 55 %. Results: She was diagnosed to be a case of Sickle Cell disease. But Sickle cell disease is usually associated with leukocytosis with left shift & thrombocytosis. But our hematological picture was pacytopenia. Finally bone marrow aspiration was done and showed highly cellular aspirate with total replacement of the marrow by the abnormal hypergranular promyelocytes with classical faggot cells. The trephine biopsy showed near total replacement by sheets of immature myeloid cells. A diagnosis of APML was made. PML-RARA testing by gel PCR was positive for bcr 1 isoform. The patient was treated with ATRA. Now the patient is doing well. Conclusion: To the best of our knowledge this is the first case in literature of concurrent presentation of Sickle cell disease and APML and highlights the important of bone marrow examination in Hemoglobinopathy patients presenting with pancytopenia.

60. Radionuclide (MUGA) studies of left ventricular functional abnormalities in asymptomatic patients with sickle cell anemia.

1995

Indian heart journal

Pani, S and Pande, T K and Hiran, S and Vishwanathan, K A and Sood, A

Radionuclide ventriculography was performed on 10 normal subjects and 39 patients with sickle cell anemia (10 homozygous and 29 heterozygous sicklers) at rest and after exercise. Their left ventricular (LV) function was assessed in both these situations. The results were then compared within the subgroups. The reduction in ejection fraction (EF) response (47.5 +/- 7 at rest and 46.4 +/- 8 at exercise in homozygous patients, and 52.4 +/- 8 at rest and 54.3 +/- 8 at exercise in heterozygous patients) was significant in both the homozygous and the heterozygous groups but more so in the former group. The diastolic filling was also significantly impaired in the homozygous group (PER 2.64 +/- 0.74, PFR 2.13 +/- 0.42 and PFR/HR 0.014 +/- 0.001). The study statistically demonstrates, that LV filling patterns are altered in the sickle cell patients, even in the absence of clinical symptoms relating to LV dysfunction. This fact may prove to be a marker of sickle cell heart disease. Frequent and significant sickling is probably the cause of more pronounced LV functional abnormalities in homozygous sicklers.

61. Integrative microRNA and gene expression analysis identifies new drug repurposing candidates for fetal hemoglobin induction in Î²-hemoglobinopathies

2019

Gene

Das, S S and Sinha, R and Chakravorty, N

Therapeutic induction of fetal hemoglobin (HbF) is one of the most promising approaches to ameliorate the severity of hemoglobinopathies like Î²-thalassemia and sickle cell anemia. Although several pharmacological agents have been investigated for HbF induction in adults, the majority of these are associated with significant side-effects. While drug repurposing is known to open new doors for the use of approved drugs in unexplored clinical conditions, the primary challenge lies in identifying such candidates. In this study, we aimed to identify repurposing candidates for HbF induction using a novel in silico approach utilizing microRNA-pathway-drug relationships. A computational drug repurposing strategy identified several unique candidates for HbF induction; among which Curcumin, Ginsenoside, Valproate, and Vorinostat were found to be most suitable for future trials. This study identified new drug repurposing candidates for HbF induction and demonstrates an easily adaptable methodology that can be used for other pathophysiological conditions.

62. Approach to dysfunction of hemoglobin: Case reports

2016

Turkish Journal of Biochemistry

Oktay, G

Hemoglobin molecule contains 4 heme groups and 1 globin. Each of 4 heme is made from protoporphyrin III and Fe2+. In polypeptide chains can be found various types of hemoglobin, including Î±-chain, Î²-chain, Î³-chain, Î´-chain. In erythrocytes of adults are found HbA1, HbA2, HbF. HbA1 contains about 97-98%, HbA2 from 0.5%-2.5%, HbF makes up to 1% of total hemoglobin. Abnormal hemoglobin causes various pathologies: 1) new amino acids can be inserted into the polypeptide chains of hemoglobin or be substituted. 2) may be caused a defect in production of globin chain; proper globin chains are not produced. 3) combination of type 1 and type 2 is possible too. 4) Hereditary persistence of fetal hemoglobin (HPFH); asymptomatic. In the World are known 1189 abnormal forms of hemoglobin. Turkish organization â€œAltay ve Akarâ€ listed them and published. According to this, most common hemoglobin mutations in our country are Hb S, Hb D, Hb E and Hb O-Arab. Thalassemia: microcytic hypochromic anemia. Hereditary hemolytic disease; the most common diseases seen in humans single gene disorder, normally Î± and Î² chains are synthesized harmonically but disease disbalances synthesis. Î²-thalassemia sometimes reduces synthesis of Î²-chain; Î±-chain synthesis stays normal. When there is a single gene disorder, form of disease is called â€œÎ²-thalassemia minorâ€, disorder of two genes -â€œÎ²-thalassemia majorâ€. Patients, who have severe form of anemia, are required to take regular blood transfusion during their first years of life; therefore, depending on the iron overload in the blood (hemosiderosis), patients are scheduled for transfusion. The complexity of disease mainly is related to the degree of imbalance between Î± and Î² chains. Hb H and Hb Barts: Hb H, does not include Î±-chain globin but is contained from 4 Î²-chains of hemoglobin. Hb Bart's globin also has not Î± -chains and contains 4 Î³ -chain of hemoglobin. Hb H and Hb Barts can be detected in the blood of Î± -thalassemia patients. Each globin gene, which is located in the 16th chromosome, has 4 copies. It is expressed like (Î±Î±/Î±Î±). When gene disorder is ([Î±+â†'(-Î±/Î±Î±)], it is called â€œsilent carrierâ€. Blood counts are normal. Slight hypochromia and microcytosis may be evident, normal Hb A2 and Hb F levels. If there are two defects in globin genes [(Î±+/Î±+â†'-Î±/-Î±) , (Î±0â†'-/Î±Î±)] disorder is called â€œ thalassemia trait Î±â€. Possibility to have hypochromic erythrocytes and microcytes which can cause mild anemia. Disorder of three globin genes [Î±+/Î±0â†'-Î±/-] is â€œhemoglobin H diseaseâ€; microcytic, hypochromic, hemolytic anemia, mild hepatosplenomegaly, jaundice and can be observed. If all four globin genes are defected [Î±0/Î±0â†'-/-] it is called â€œhydrops fetalisâ€. Î± globin chains are needed for the formation of HbF. In this way Hb A2

and Hb F are synthesized. Hemoglobin level is significant index. When level is 3-8 g/dL hepatosplenomegaly, skeletal and cardiac disorders, abdominal infections and severe clinical symptoms such as severe anemia or edema are observed. These patients are lost after birth or unborn fetus dies during the pregnancy; Sickle cell anemia (HbS, Î²6 Glu-Val): autosomal recessive inherited. Occurs during hemolytic anemia in homozygous. Heterozygous carriers are asymptomatic. Sickle cells are collected in spleen, they break the circulation, vascular congestion causes the pain. HbE (Î²26 Gluâ†'Val): HbE is common in Southeast Asia. Homozygous patients, can have a hemolytic anemia and mide enlargement of the spleen, often confused with iron deficiency anemia. Cells are detected in peripheral blood smear. There are not clinical disorders in HbE heterozygote. At the same time in HPLC Hb A2 and Hb E can be found. HbE-beta thalassemia: Hb E syndrome clinical symptoms are the most severe. However, depending on Hb F level and Î±-thalassemia mutation, Î²-thalassemia can be modified (changes of phenotype). Clinical course is very heavy, especially for Î²0-thalassemia & HB heterozygote patients. HbD Punjab: Punjab is the region of India, and this type of disease is mostly common there (2%). By the survey conducted in Turkey, this ratio was found as 0,2%. Heterozygotes have clinical diseases. Homozygous patients can have mild anemia. Patients need a prenatal diagnosis and treatment. Hb SD disease: causes severe clinical symptoms. If patients have acute chest syndrome, stroke, anemia, joint necrosis then symptoms such as sequestration crisis intensifies. As a result we can see sickle cell anemia. HbC (Î²6 Gluâ†'Lys): HbC electrophoresis results are similar to Hb A2. This disease is common in West Africa (28%). It is also common in America. Clinical course is not severe. Most of the abnormal hemoglobin variants in Turkey are variants of Hb S. Also, in our country we have widespread Î± and Î² mutations, so it is important to make the correct identification to cure properly. Blood is analyzed for RBC, Hb, Hct, MCV, MCH, MCHC, Hb A2 and Hb F. Attention is paid to MCV and MCH. If MCV< 80fl or MCH<27pg, mutation could be diagnosed. Also, when electrophoresis shows high level of Hb A2, person is accepted as Î²-thalassemia carrier. Usually, having an Î±-thalassemia, Hb A2 level is normal and other different researches are needed to diagnose this disease.

63. Mutational spectrum of b globin gene in transfusion dependent patients from central India

2019

Vox Sanguinis

Shrivastava, M and Bathri, R and Chaterjee, N

Background: Thalassaemia and related hemoglobin disorders are one of the most common genetic disorders among humans. These disorders entail huge morbidity, economic and psychological burden on the families of the affected. Genetic counseling and prenatal diagnosis are the steps that can help reduce this burden. Presently there is a paucity of data on mutational spectrum of thalassaemia from central Indian region. Aims: The study was undertaken in a tertiary care hospital to determine the mutational spectrum of beta globin genes in a city from Central India. Methods: Blood samples were collected from 62 transfusion dependent patients demographic and relevant data was collected and screened for the five common Indian beta thalassaemia mutations IVS1-5 (G-C), IVS1-1(G-T), Cd41/42 (-TCTT), Cd8/9(+G), 619 bp deletion and two rare mutations -88 (C-T) and CAP+1 (A-G) using ARMS PCR and GAP PCR technique. In addition, we also didPCR for rare hemoglobin disorder like Hb Lepore and dbchain disorder by GAP PCR. Results: Out of 62 transfusion dependent patients enrolled for the study, 42 were males and 20 females. The average age of the subject was 8 years. The age at first diagnosis of the disease ranged from 6 months to 3.5 years. The frequency of transfusion was in the range of 15 days to one month in all the cases studied. IVS I-5 (G-C) (46%) was the most common mutation followed by IVS I-1(G-T) (12%) and 619 bp (9%). Amongst the abnormal hemoglobin sickle cell (HbS) and HbE were found at 4% and 3% of all the loci studied. We also report two loci with Hbdb and one locus with Hb Lepore in the present sample. Overall 93.5% of the mutations could be identified. Summary/Conclusions: The results highlight that besides the common Indian mutations, a few rare mutations and abnormal hemoglobin are present in the genotype of transfusion dependent patients in Bhopal which imply to include these traits during prenatal diagnosis. Identification of the exact mutation helps to define the severity of the phenotype, plan therapy and form the basis of comprehensive diagnostic database that would be useful not only for genetic counseling but prenatal diagnosis as well.

64. Sickle cell anaemia presenting as inflammatory polyarthritis

2014

Indian Journal of Hematology and Blood Transfusion

Ballikar, R and Sinha, N and Dibyendu, D and Bhattacharya, D and Bhattacharya, S and Nath, U K and Bhattacharya, M

Summary: This is a case report of a young male presenting with inflammatory polyarthritis as the sole manifestation of sickle cell disease and who was misdiagnosed and treated outside as a case of rheumatoid arthritis. Introduction: Sickle cell anaemia is a hemoglobinopathy which predominantly presents in early childhood with features of hemolytic anaemia and painful crises. Case Discussion: A 27-year-old male patient presented with history of recurrent episodes of painful swelling of large and small joints of all four limbs associated with morning stiffness, without axial skeleton involvement. The patient also had chronic pain in both the hip joints and bursitis of knee joints. Patient was investigated for polyarthritis for 3 years. Rheumatoid factor and antinuclear antibody were positive and CRP was elevated. X rays of hands and feet done revealed erosive arthritis, with patchy areas of osteosclerosis and osteopenia. Patient was labeled as having rheumatoid arthritis and treated with hydroxychloroquine. When his hip pain worsened with restriction of movements, X ray of the hip joint revealed bilateral loss of femoral head, which was later by MRI confirmed to be avascular necrosis. Retrospectively, patient gave history of intermittent jaundice, but there was no history of blood transfusion. On examination there was no organomegaly. Hemogram with peripheral smear revealed sickled red cells. Hemoglobin HPLC revealed Homozygous Sickle cell disease. Both parents had HbS carrier state. Patient was started on therapy with Hydroxyurea, with symptomatic treatment of the painful crisis with analgesics and hydration. Patient is currently doing well with marked reduction of his musculoskeletal complaints. For the avascular necrosis, bilateral Total hip Replacement has been done. Conclusion: Sickle cell anaemia may present only with arthropathy or arthritis with no other evidence of hemolytic disease. This should be kept in the differential diagnosis of musculoskeletal disorders whenever applicable. Early and prompt diagnosis will result in preventing or limiting the debilities associated with this disease.

65. Haemoglobin-D disease (Iran subtype) in adult male: Rare case report

2020

Indian Journal of Hematology and Blood Transfusion

Waingankar, H S and Taori, B and Shukla, M and Kejriwal, A

Aims & Objectives: To report a rare case of hemoglobin-d disease(Iran subtype) in adult male. Patients/Materials & Methods: Hemoglobin D [Hb D]is a rare form of hemoglobinopathy in homozygous form. The heterozygous disease is silent clinically. A 50 year old male presented to the Emergency Room of MGM Medical College and Hospital, Kamothe, Navi Mumbai, with chief complaints of giddiness since four days and right shoulder pain with yellowish discoloration of sclera for a period of three months. On examination the patient had severe pallor and icterus. Peripheral smear showed dimorphic anemia with thrombocytopenia and High performance liquid chromatography [HPLC] was suggestive of Hb D Iran subtype. Results: Peripheral smear showed Dimorphic anemia with thrombocytopenia with microcytic hypochromic and normocytic normochromic RBCs with anisopoikilocytosis and occasional tear drop cells. A High performance liquid chromatography [HPLC] of haemoglobin done was suggestive of Hb D Iran. Discussion & Conclusion: Discussion: Itano in 1951 first found a group of hemoglobinopathies in a white family and named it as Hemoglobin D (Hb D) [3]. Later, Rahbar found a substitution of Glutamic Acid + Glutamine (GAA + CAA) at b22 and classified it as Haemoglobin D-Iran (Hb D-Iran) [4].It should be noted that three other substitutions have been described at b22 position viz. E Saskatoon (Lys), G Coushatta (Ala) and G Taipei (Gly) [5].In India, both the homozygous and heterozygous forms of the disease are very rare. In homozygous cases, such as one reported by Thornburg CD et al., Hb D-Iran can present with anaemia, poikilocytosis and mild hemolysis [1]. In heterozygous forms the patient remains clinically silent and hence the case is missed and remains undetected. A case has been reported by Agrawal MG et al., where Hb D-Iran was coexisting with Î²-Thalassemia [6]. Another case was reported by Gupta et al., where Hb D-Iran was

present along with Hb D-Punjab [2].The diagnosis still remains an incidental finding and may remain undetected unless it presents with symptoms of other co existing hemoglobinopathies like thalassemia, sickle cell disease etc. When identified,genetic sequencing still remains the gold standard. As most cases are silent clinically, no active intervention is required for the disease.Conclusion: Hemoglobin D Iran subtype is a very rare form of hemoglobinopathy. It is mostly an incidental diagnosis when a patient presents with complaints due to other common hemoglobinopathies for example thalassemia. With newer and relatively easier technologies like capillary electrophoresis the diagnosis of HbD disease will become less cumbersome. However genetic sequencing plays important role in diagnosis. In above case patient presented with lone diagnosis of Hemoglobin D Iran subtype it was not associated with any other hemoglobinopathy.

66. Clinical and molecular characterization of 194 cases of sicklebeta thalassaemia in western odisha and their response to hydroxyurea therapy

2012

Indian Journal of Hematology and Blood Transfusion

Dehury, S and Patel, D K and Patel, S and Purohit, P and Bishwal, S C and Meher, S and Padhan, B and Das, K

Introduction: Hemoglobin Sickle-Î²-thalassaemia is a variant form of sickle cell disease, resulting from the inheritance of HbS and b-thalassemia genes. Objective: To study the clinical, hematological and molecular profile of sickle-Î²-thalassaemia double heterozygotes in western Odisha. Materials and Methods: 194 cases of HbS-b-thalassemiawere studied at Sickle Cell Clinic, VSS Medical College Hospital, Burla, Odisha, India. Cases were diagnosed by CE-HPLC (BioRad Variant II) and family study and confirmationwas done by ARMS-PCR. a-Thalassaemia was studied by GAP-PCR. Cases with severe clinical features were treated with Hydroxyurea at a dose of 10 mg/kg body wt/day orally. Results: Three bthalassaemia mutations >IVS1-5(G-C), FS41/42(-CTTT), codon 15 (G>A)] accounted for 97 % of all HbS-Î²-thalassaemia cases. IVS1-5(GC) was the commonest mutation (184/194, 94.85 %). The mean %HbA2, %HbF and %HbS were 5.02 Â± 0.86, 19.04 Â± 8.89 and 69.84 Â± 9.91 respectively, whereas the mean RBC, MCV and MCH were found to be 3.90 Â± 0.98 9 103/Î¼l, 71.68 Â± 9.48 fl and 23.72 Â± 8.94 pg respectively. Commonest clinical presentation was splenomegaly (39.69 %) followed by hepatomegaly and AVN (23 and 7.2 % respectively). 57.21 % had severe anaemia (Hb below 9 g/dL). Deletional Î±-thalassemiawas found in 25 %of cases. 64.43 % patients with VOC more than 3/year and BT more than 2/year were treated with hydroxyurea.Conclusion: IVS1-5(G-C) mutation was the commonest and found in 94.85 % of cases. FS41/42(-CTTT) and codon 15 (G>A) mutations were reported for the first time fromthis region. a-Thalassaemia had no significant effect on the clinical and hematological features except that HbF was significantly high in a-thalassaemia group. Low dose Hydroxyurea had an ameliorating affect on the clinical and hematological profile of HbS-Î²-thalassaemia patients in western Odisha.

67. Fibrinogen in sickle cell disease; an immunohaematological study

1982

Indian Journal of Pathology and Microbiology

Saoji, A M and Gupta, V L and Dube, G L

The study includes 83 cases of sickle cell disease and 100 individuals as controls. The cases were further divided into non-crisis and crisis by the standard criteria. Fibrinogen estimation was done by radial immuno diffusion, by raising the monospecific antiserum in the local laboratory. Fibrin plate and euglobulin clot lysis time was done as parameters of fibrinolysis, in selected cases. Follow-up was done in 5 cases. It was observed that cases of vaso occlusive crisis showed both hyper-fibrinogenemia (460-800 mg %) and hypo-fibrinogenemia (50 mg %). Normals showed a range from 220 to 310 mg %. High levels were associated with development of thrombotic manifestations due to hyper-viscosity, causing unfavourable rheological conditions. One case with 50 mg % terminated in disseminated intra-vasculation (DIC). Non-crisis cases showed a normal pattern. Follow-up showed

basal levels after the termination of crisis phase. It is felt that serial estimations of fibrinogen might prove to be useful as a prognostic parameter, in the sickle cell crisis. The present immunological technique proved to be specific, sensitive and reproducible.

68. Hematological profile and clinical severity scoring in E-beta thalassemia

2014

Indian Journal of Hematology and Blood Transfusion

Murari, M and Pani, K C and Sharma, S and Agrawal, S and Phadke, S

Background: Hemoglobin E, a structural hemoglobin variant is themost common hemoglobin variant in South East Asia and the second most hemoglobin variant worldwide. In addition compound heterozygous states occur such as hemoglobin E/b Thalassemia (E/b thal) and rarely sickle cell/hemoglobin E disease (SE genotype). Patients and Methods: Present study includes clinico-hematological findings in 20 cases of Hb E-beta thalassemia diagnosed within 1 year period. All patients had detailed clinical, and hematological examination and HPLC. Mutational analysis was done in 12 patients. Clinical severity was assessed according to the scoring system by Sripichai et al. Results: Sixteen male and four female patients with wide age distribution (1 year to 38 years) were diagnosed as E-b Thalassemia, on the basis of HPLC and molecular findings. Thirteen patients had severe anemia and seven had moderate anemia at presentation. Significant negative correlation was seen between Hb E and red cell indices (MCV and MCH). Significant positive correlation was also observed between Hb E and RDW. We stratified the patients into mild, moderate and severe category according to the scoring system. Patientswith severe disease showearlier age of presentation, more dependency on transfusion, larger spleen size and lower hemoglobin at presentation, however there were no statistically significant differences in the hematological parameters between the three groups. Conclusions: Hemoglobin E-beta Thalassemia results in chronic hemolytic anemias with variable clinical severity, most of the cases required regular transfusions. In our study we did not find statistically significant correlation of haematological findings with clinical severity scoring.

69. Genetic association of GSTM1, GSTT1, and GSTP1 polymorphisms with sickle cell disease complications: A systematic review and meta-analysis

2020

Meta Gene

Verma, H K and Swarnakar, S and L.V.K.S., B

Background: Sickle cell disease (SCD) is a monogenic blood disorder characterized by vaso-occlusive crises (VOC) also recurrent episodes of severe pain. Glutathione S-transferase enzyme plays a crucial role in the defense mechanism of cells and tissue damage from oxidative stress during vaso-occlusive crises. Polymorphic variants in the GSTT1, GSTM1, and GSTP1 genes are known to influence glutathione enzyme activity and modulate the clinical severity of SCD. Objectives: We conducted a meta-analysis to synthesize evidence and to assess the relative impact of GST gene polymorphisms on SCD risk. Methods: Comprehensive search in the PubMed, Google Scholar, EMBASE, Chinese National Knowledge Infrastructure (CNKI) and the Web of Science Databases was conducted to identify the relevant studies. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to estimate the strength of association between GST polymorphisms and SCD risk. The Cochrane Q and I2 statistics were used to detect heterogeneity. Funnel plots and Egger â€˜s test were used to estimate the publication bias. Results: Eight studies involving 394 SCD patients / 593 controls of GSTM1, 397 SCD patients / 595 controls of GSTT1, and 178 SCD patients / 178 controls of GSTP1 polymorphism were ultimately considered for meta-analysis. Pooled analysis of GSTT1 (OR = 1.814; 95% CI: 1.34â€“2.45; P < 0.001) and GSTP1 (OR = 1.746; 95% CI: 1.42â€“2.66; P < 0.010) polymorphisms revealed significantly increased risk of complications in SCD, while GSTM1 null genotypes (OR = 0.867, 95% CI: 0.633â€“1.189; P < 0.376) did not show association with SCD complications. Significant between study heterogeneity (I2 > 50%) was observed for in all three polymorphisms (GSTM1 = 68.7%), (GSTT1 = 71.6%), (GSTP1 = 83%). Conclusion: The carriers of

GSTT1 null allele and GSTP1 Val allele are associated with the increased risk of SCD complications. However, GSTM1 deletion allele is not associated with the risk of SCD complications. A large number of studies must be evaluated for a more precise association of these polymorphisms.

70. Sudden and unexplained death in an infant: Sickle cell crisis

2012

Journal of Clinical and Diagnostic Research

Nikumbh, D B and Jagtap, S V and Mali, R K and Jain, G and Khatib, W

Sickle cell syndromes are remarkable for their clinical heterogeneity, including their presentations as sudden and unexpected deaths due to a sickle cell crisis. Such cases are accompanied by various provocative factors like exertions (exercise), dehydration, hypoxia, and infections. The sudden and unexpected death of an apparently healthy baby is a tragedy for its parents, grandparents and siblings and for the paediatrician. At the same time, these deaths are challenges for the forensic and paediatric pathologists. We present here, a rare case of sudden and unexpected death in a 3-month old infant with undiagnosed sickle disease, which was not preceded by any provocating factor. We are presenting this case to emphasize that sickle cell crisis is one of the causes of sudden, unexplained infant deaths and to the highlight the role of autopsy in such cases

71. HbD - Punjab associated with HbS: A report of two cases from India

2000

Indian Journal of Hematology and Blood Transfusion

Panigrahi, I and Agarwal, S and Signhal, P and Phadke, S and Agarwal, S

Double heterozygosity for HbS {(Î²6(A3) Gluâ†'Val); Tâ†'A} and HbD {Î²121 (GHu) Gluâ†'Gln; Gâ†'C} is reported to have severe manifestations comparable to homozygous sickle cell disease. Here, we report one male & one female patient with hbSD aged 18 years and 23 yr. respectively at presentation. Case 1 had recurrent attacks of jaundice and case 2 had significant short stature with recurrent biliary colic. Thus, the presentation of HbSD disease can be variable. Laboratory diagnosis of HbSD is difficult HbD has electrophoretic mobility similar HbS at alkaline pH & at acidic pH 6.2, it migrates with HbA. However, with the help of HPLC analysis & molecular analysis it is possible to establish the mutation at Co6 (Tâ†'A) & Co121 (Gâ†'C). The clinical implications and the importance of early detection and prenatal diagnosis are discussed.

72. The effect of pre G Î³globin gene haplotype on the clinical severity of thalassemia and sickle cell patients

2011

Indian Journal of Hematology and Blood Transfusion

Dabke, P and Colah, R and Ghosh, K and Nadkarni, A

Introduction: Different raised HbF determinants act as genetic modulators of Sickle Cell Disease. Well documented among them is the XmnI polymorphism. Recently it has been shown that the TAG Pre G Î³ globin gene haplotype is associated with raised HbF levels and helps in reducing the severity of Sickle Cell Disease. Our aim was to look for the effect of TAG haplotype on the disease severity of thalassemia and sickle cell anemia (SCA) patients. Materials & Methods: The patient groups comprised SCA-10, HbS-Î² thalassaemia- 9, Î² thalassaemia intermedia-37 and Î² thalassaemia major-40. XmnI polymorphism was studied by PCR-RFLP technique. The Pre G Î³ globin haplotypes were determined by PCR-DNA sequencing (polymorphic positions studied 7rarr; -1450, -1280 and -1225). Results: The XmnI polymorphism (+/+) was present in all the sickle homozygotes and in 32.43% of thalassemia intermedia patients. Three haplotypes TAG, TGG and TGA were seen. All the SCA patients showed homozygosity for the haplotype TAG which is associated with raised HbF. In

the thalassemia intermedia group, TAG/TAG genotype was found in 40.54% cases as against only 10% of the thalassemia major patients. Conclusions: The Pre G Î³ globin gene haplotype TAG along with XmnI polymorphism seems to modulate the disease severity. These factors might have contributed for milder clinical presentation of our thalassemia intermedia and SCA patients.

73. Klebsiella pneumoniae--an emerging bacterial cause of osteomyelitis in sickle cell disease.

1999

The Journal of the Association of Physicians of India

Hiran, S and Vishwanathan, K A

Salmonella species is the accepted organism causing osteomyelitis in sickle cell disease. Klebsiella pneumoniae is now emerging as a new etiological agent. We report a case of sickle cell osteomyelitis due to Klebsiella pneumoniae.

74. Pro-oxidant and anti-oxidant status in patients of sickle cell anaemia

2004

Indian Journal of Clinical Biochemistry

Titus, J and Chari, S and Gupta, M and Parekh, N

The role of oxidant damage to red cells in sickle cell anaemia has been of interest in recent years. Although, available reports suggest that sickle cell erythrocytes are susceptible to endogenous free radical mediated oxidant damage there remains discrepancy in the status of antioxidant enzymes and antioxidant vitamins in these patients. In view of this, 107 cases of sickle cell anaemia (36 'SS' and 71 'AS' pattern - as confirmed by haemoglobin electrophoresis) were subjected to analysis of malondialdehyde, ascorbic acid, superoxide dismutase and albumin. The results were compared with 54 age and sex matched healthy controls. The results indicate a marked increase in lipid peroxidation and superoxide dismutase levels in both 'SS' and 'AS' types of sickle cell anaemia as compared to controls. Although no difference was observed in the levels of albumin in these groups, the levels of ascorbic acid were significantly depleted in sickle cell anaemia patients. The results are indicative of enhanced lipid peroxidation along with imbalance in the pro-oxidant and antioxidant status in patients of sickle cell anaemia.

75. Diagnosis of sickle cell disease at autopsy: A case report

2011

Indian Journal of Forensic Medicine and Toxicology

Bardale, R and Dixit, P and Yadav, S

Individual suffering from sickle cell disease may present to forensic pathologist as a case of sudden death. The postmortem diagnosis of SCD related death is often difficult because of failure to anticipate the presence of such disorder. In addition, actually making the diagnosis of sickle cell crisis as a cause of death is confounded by the likelihood of antemortem, perimortem or postmortem sickling unrelated to the cause of death. In this communication we are presenting the findings related to the diagnosis of SCD at autopsy by using hemoglobin electrophoresis. In the present case, we are able to obtain result up to 5 hours postmortem interval.

76. Molecular diversity in genetic hematological syndromes in India

2013

Indian Journal of Hematology and Blood Transfusion

Tamhankar, P

The molecular studies on beta thalassemia and classic hemoglobinopathies such as sickle cell disease have been the early beginnings of genetic hematology in India. This group of disorders has been recognized by the World Health Organization as a public health concern owing to increased childhood mortality and morbidity (WHO, 2008). About 10 % of the total world thalassemia patients belong to the India subcontinent and the carrier rate is 3-4 % on an average (Panja et al. 2012). In the beginning, elaborate studies in migrant population in UK and USA established the presence of thalassemia mutations in Gujaratis, Punjabis and Sindhis. However, with follow up collaborative studies undertaken in different studies from India, the wide distribution and extensive heterogeneity in different Indian sub-populations became apparent (Sinha et al. 2009). With the recognition of several other hematological syndromes both common and rare and the increase in state-of-the-art centers with genetic testing facilities, the mutation database for genetic hematological conditions has seen a great increase in its stock. Allelic and Genetic heterogeneity The beta globin gene is located on chromosome 11 and comprises of three exons. The primary protein produced is 147 amino acids long. The beta globin mutation database HbVar lists 830 unique sequence variants in the beta globin gene leading to variant hemoglobins or thalassemia. A metanalysis collated data on 8,505 beta globin alleles from 17 studies in India and concluded that there were 64 unique disease causing mutations, The most common mutation is IVSI- 5(G>C) and represents 54.7 % of all Ã¢-thalassaemia mutations reported. IVSI-5(G>C), 619-bp del, IVSI-1(G>T), Codon 41/42(- TCCT) and Codon 8/9(+G) comprises the five most common disease mutations l and totals 82.5 % of all mutations, with Codon 15(G>A), Codon 30(G>C), Cap site +1(A>C), Codon 5(-CT) and Codon 16(- C) accounting for an additional 11.0 % of all mutant alleles (Sinha et al. 2009, Tamhankar et al. 2009). However, the nationwide data may not hold true for smaller inbreeding populations in India since around 50 % of the above data has originated from North Punjab, west Maharashtra and west Gujarat. The high percentage of - 88(C>T) alleles in cases from Punjab (74.3 %) is ascribed to the frequency of this mutation in the Jat-Sikh community (Garewal et al. 2005). Likewise, the high prevalence of Codon 5(-CT) in Gujarat (79.7 %) is associated with the Lohana and Prajapti communities in that state (Sheth et al. 2008). Although the Poly A(T>C) allele has been reported in the populations of nine states, 65.6 % of cases were subjects who originated in the adjacent southern states of Tamil Nadu and Karnataka (Colah et al. 2009). Osteopetrosis is a group of genetic disorders characterized by increased bone density leading to progressive bone marrow failure due to obliteration of bone marrow cavity. There is considerable genetic heterogeneity with mutations being possible in one of nine genes. Mutations in TCIRG1 gene account for 50 % of infantile malignant cases worldwide and also from India (Phadke et al. 2011; Tamhankar et al. 2013 unpublished observation). Most of the mutations are private and they occur throughout the length of gene making screening for mutations difficult. Founder Effects and their Implications on Public Health In genetic, founder mutation is a mutation present in a population derived from one or more individuals who have been the founding ancestors of that population. Several communities practice endogamy which tends to concentrate the mutations in descendants leading to disease. Recognition of these mutations is not only important for cost effective and rapid diagnosis of affected individuals but also essential for population screening and reduction of burden of disease. Kasatkar et al. identified the c.6187C>T (p.P2063S) mutation in homozygous state in 11 unrelated patients of von Willebrand disease (VWD) from Gujarat belonging to Kachi Modh Ghanchi community. Haplotype analysis concluded that this is a founder mutation in this community. This variant was reported both as polymorphism and pathogenic mutation in VWD databases. However, segregation analyses in the 11 families from Gujarat clearly demonstrated disease in homozygous individuals and heterozygous state in carrier parents. Bioinformatic analyses in addition supported the pathogenic nature of this variant. This example proves that epidemiology data can improve understanding of molecular pathophysiology of disease. Panethnic Molecular Phenomena Certain regions of the genome and certain genes are more disease prone owing to their peculiar structure or sequence. Such mutations are usually panethnic and hence molecular diagnosis for the resulting diseases follows a targeted approach. The dinucleotide CpG islands is a hotspot for mutation in the human genome as a result of the modification of the 50 cytosine by cellularDNAmethyltransferases and the consequent high frequency of spontaneous deamination of 5-methyl cytosine (5mC) to thymidine. Several hematological diseases can be explained by the cytosine to thymine mutation (C>T). Dyskeratosis congenita (DC) is a bone marrow failure syndrome classically associated with a triad of mucocutaneous features: nail dystrophy, oral leukoplakia, and abnormal reticulate skin pigmentation. There is genetic heterogeneity with mutations being identified in either of the following genes DKC1, TERC, CTC1, TERT, TINF2, NHP2, NOP10, and WRAP53. The mutation c.1058C>T (p.A353V) in DKC1 gene is the commonest mutation in patients with dyskeratosis congenita and occurs due to this mechanism. This has been

demonstrated in a child in our study (Tamhankar et al. 2010). Similarly the denovo heterozygous mutations p.R282H and p.R282C in TINF2 gene also occur in a CpG hotspot region. The R282H has also been identified in another Indian child (Tamhankar et al. 2013 unpublished observation). Griscelli syndrome type 2 (GS2) is a rare autosomal recessive disease characterised by pigmentary dilution of skin and hair, variable cellular immunodeficiency and an acute phase of uncontrolled T lymphocyte and macrophage activation leading to fatal hemophagocytic syndrome Mutations in RAB27A gene are responsible for GS2. The mutation c.C550T (p.R184X) accounts for 30 %of mutations leading and this has been demonstrated in 10 unrelated patients from India (Tamhankar et al., unpublished data 2013). Several genes have dysfunctional relatives that are lost their protein coding ability and hence aptly named pseudogenes. Their presence alongside the gene leads to increased susceptibility to genomic rearrangements during meiotic recombination leading to disease. Most pseudogenes are created by one of two mechanisms: tandem duplication or retrotransposition from a functional gene. One such tandem duplication originated the GBA pseudogene (psGBA), the nonfunctional duplicate of the GBA gene, which encodes for the glucocerebrosidase protein. Mutations in GBA produce Gaucher disease, which is an autosomal recessive lipid storage disease characterized by deposition of glucocerebrosides in cells of the monocytemacrophage system. Bisariya et al. (2011) identified common GBA mutations (L444P, N370S, IVS2 and D409H, and 55Del) in approximately 50 % of Indian patients. The commonest mutation L444P can result from either reciprocal recombination or gene conversion with the nearby glucocerebrosidase pseudogene. The L444P point mutation was identified as the commonest mutation in our study of 15 Gaucher disease patients (Tamhankar et al., unpublished study, 2013). Conclusion The molecular basis of genetic hematological diseases is complicated by allelic heterogeneity. However, identification of founder mutations/ recurrent mutations makes rapid and cost effective diagnosis possible.

77. Study of certain biochemical parameters in bone diseases with special reference to sickle cell anemia

2016

Indian Journal of Public Health Research and Development

Rajesh, T and Pankaj, T and Prashant, N and Sadhana, B

Background: The vasoocclusive process of sickle cell disease causes bone infractions, Osteomyelitis, Arthritis and many more complications. Inflammatory markers and other biochemical parameters could be explain the actual reason and proved helpful to overcome these complications. Method: In this study we performed CRP, IL-6, TNF-a, Homocysteine along with other routine biochemical parameters in 30 Sickle cell patients presented with various bone complications and compared them with 30 age matched normal subjects. Result: We found increased level of all inflammatory markers when compared to control group along with disturbed biochemical profile. Conclusion: We concluded that high level of Inflammatory markers also predicts status of bone complications and helpful to assess the condition of patients.

78. Giant oral tumor in a child with malnutrition and sickle cell trait: Anesthetic challenges

2013

Journal of Anaesthesiology Clinical Pharmacology

Singh, P M and Borle, A and Trikha, A

Pediatric oral tumors have always been challenging for the even most skilled anesthesiologists. The conventional method of awake intubation is not realistic in this age group. The management is to chart out a plan to intubate the child post induction. We describe successful management of a case of giant of ossifying fibroma in a child with sickle cell trait where non-conventional innovate approach helped us to secure the airway pre-operatively and avoid possible medical complications.

79. Gross hematuria in sickle cell trait patients

1999

Nederlands Tijdschrift voor Urologie

Van Den Ouden, D and Eland, D

Gross hematuria occurs in 3-4% of the patients with sickle cell trait. In these patients no other cause for the hematuria is detected beside the sickle cell trait. Predisposing factors in the renal medulla (hypoxia, hypertonicity, acidosis) promote the sickling of erythrocytes. This causes several nephropathies, of which unilateral hematuria is the most common. Certain groups in the population carry a relatively high risk for sickle cell trait (African en India origin, Mediterranians). In a patient of these risk- groups with hematuria of unknown origin, Hb-electrophoresis should be done to detect sickle cell trait. In the present study a patient with hematuria and sickle cell trait is presented. A review of the literature is performed concerning the etiology, epidemiology, symptoms, diagnosis and therapeutic possibilities in this disease.

80. Gallstones in patients with inherited hemolytic diseases

2015

International Journal of Pharmacy and Pharmaceutical Sciences

Abdullah, U Y H and Jassim, H M and Baig, A A and Khorsheed, R M and Al-Khayat, A M H and Sulong, A F B and Abed, N F and Yassin, W A

The purpose is to provide an overview on the incidence of gallstone disease in patients with various types of inherited (chronic) hemolytic diseases at risk of cholelithiasis/choledocholithiasis with particular emphasis on its pathogenesis, genetic, risk factors and management. A detailed electronic literature search to determine the source of materials for this review article was done. The reported incidences of gallstones and choledocholithiasis vary according to the different types of inherited hemolytic diseases and the ethnicity of the studied populations. To date, no review article summarises the incidences of cholelithiasis in patients with various inherited haemolytic diseases was published. Regular ultrasound examination for the presence of gallstones recommended in patients with inherited haemolytic anaemias, particularly those with additional risk factors recommended. Further studies for evaluating the reasons for the higher incidence of cholelithiasis in thalassemia major and sickle cell anemia compared to hereditary spherocytosis; the effect of co inheritance of alpha thalassaemia on decreasing bilirubin level in patients with sickle cell disease and beta thalassaemia; the effect of the co inheritance of UGT1A1 and ABCG8 gene mutation on the incidence of gallstones in other blood diseases such as Hb-H disease, autoimmune haemolytic anaemias, congenital dyserythropoietic anaemia, hereditary elliptocytosis, Southeast Asian Ovalocytosis, glucose-6-phosphate and pyruvate kinase deficiency are recommended. Evaluation of the potential role of the solubility of the mutant proteins and haemoglobin subunit in the red blood cells as an additional mechanism for the development of gallstones in patients with inherited haemolytic anaemias recommended.

81. Hemoglobin se disease: A case report from Kerala

2020

Indian Journal of Hematology and Blood Transfusion

Varughese, M and Das, S

Aims & Objectives: To investigate hemoglobinopathy in a diabetic with normal Hb A1c. Patients/Materials & Methods: 49 year old male,from Pathanapuram, admitted for Diabetic control presented with hyperglycemia and anemia, his Hb A1c was normal. Results: Hb 11.5 g/dl, Retic 2.33% other blood counts normal, iron status normal Blood sugar 417 mg/dl HbA1c 4.6% Indirect Bilirubin 0.96 mg/dl other biochemical parameters normal HPLC-

variant testing : Hb S 53%, Hb A2 24.4% R time 3.06. Discussion & Conclusion: Diagnosis : Double heterozygous for hemoglobin S and hemoglobin E A rare case of Hb SE disease is reported from Kerala.

82. In-silico analysis of mutations in gilbert's syndrome associated in Indian scd patients

2020

Indian Journal of Hematology and Blood Transfusion

Sachdeva, S and Bodade, A

Aims & Objectives: To analyse and compare different genotypes of UGT1A1 responsible for Gilbert's syndrome in the Indian cohort of SCD patients by in silico approach. Patients/Materials & Methods: Genotypes of 266 patients from two case control studies via Human Gene Mutation Database were curetted and comparison was carried out for different genotypes of UGT1A1 responsible for GS in the Indian SCD patients. The association between genotypes and patient's status including GS with SCD, GS without SCD versus healthy controls were evaluated and indicated through Chi square and Pearson's test. Whole analysis was performed with SPSS 25 version. p value<0.05 was considered as statistically significant. Results: On comparison of three groups of our study i.e. Gilbert's Syndrome with Sickle Cell Disease, Gilbert's Syndrome without Sickle Cell Disease compared to Healthy Controls viz three genotypes of UGT1A1 mutations were extracted from Indian SCD patients. The genotypes commonly observed were (TA)6/(TA)6, (TA)6/(TA)7 and (TA)7/(TA)7. Higher total serum bilirubin levels were found in SCD patients with the (TA)7/(TA)7 and (TA)6/(TA)7 repeats as compared with SCD patients having the (TA)6/(TA)6 repeats. Discussion & Conclusion: In this in silico analysis, we observed that sample distribution of genotypes was observed significantly associated with the different groups in the study (p<0.0001). These results will help us to know the genotype according to the patient's status.

83. A rare case report : Hemoglobin se disease from BCMCH , Thiruvalla , Kerala

2018

Indian Journal of Hematology and Blood Transfusion

Das, S and Verghese, M and Sara, R

Aims & Objectives: To investigate hemoglobinopathy in a diabetic with normal Hb A1c Patients/Materials & Methods: 49 year old male 49 year old male, from Pathanapuram , admitted for Diabetic control presented with hyperglycemia and anemia Hb A1c was normal. Results: Hb 11.5 g/dl, Retic 2.33 % other blood counts normal , iron status normal. Blood sugar 417 mg /dl HbA1c 4.6% Indirect Bilirubin 0.96 mg /dl other biochemical parameters normal HPLC - variant testing : Hb S 53% , Hb A224.4% R time 3.06. Discussion & Conclusion: Diagnosis : Double heterozygous for hemoglobin S and hemoglobin E A rare case of Hb SE disease is reported from Kerala.

84. Buccal micronucleus cytome assay in sickle cell disease

2016

Journal of Clinical and Diagnostic Research

Naga, M.B.S.S. and Gour, S and Nallagutta, N and Ealla, K K R and Velidandla, S and Manikya, S

Introduction: Sickle Cell Anaemia (SCA) is a commonly inherited blood disorder preceded by episodes of pain, chronic haemolytic anaemia and severe infections. The underlying phenomenon which causes this disease is the point mutation in the haemoglobin beta gene (HbÎ²) found on chromosome 11 p. Increased oxidative stress leads to DNA damage. DNA damage occurring in such conditions can be studied by the buccal micronucleus cytome assay, which is a minimally invasive method for studying chromosomal instability, cell death and regenerative

potential of human buccal tissue. Aim: To evaluate genomic instability in patients with sickle cell disease by buccal micronucleus cytome assay. Materials and Methods: The study included 40 sickle cell anemia patients (Group A) and 40 age and sex matched controls (Group B). Buccal swabs were collected and stained with Papanicolaou (PAP). Number of cells with micronucleus, binuclei, nuclear bud, pyknosis and karyolysis were counted in two groups as parameters for the evaluation of genome stability. Results: All the analysis was done using t-test. A p-value of <0.001 was considered statistically significant. There was a statistically significant increase in micronuclei number in SCA patients when compared with controls. Karyolytic (un-nucleated) cell number in Group A was more than to those of the controls. Conclusion: The results might suggest that patients with sickle cell anaemia have genome instability which is represented by the presence of micronuclei in the somatic cells. Presence of apoptotic cells might only indicate the bodily damage to the tissue as a result of the disease.

85. Antioxidant status and lipid peroxidation in sickle cell anaemia

2010

Biomedical Research

Hundekar, P and Suryakar, A and Karnik, A and Ghone, R and Vasaikar, M

Sickle cell anemia (SCA) is an inherited disorder of hemoglobin synthesis, characterized by life-long severe hemolytic anemia and vasoocclussive crisis. Oxidative stress play important role in pathophysiology of sickle cell anaemia. Therefore, the study was undertaken to evaluate the levels of plasma lipid peroxidation product malondialdehyde (MDA), plasma total antioxidant capacity, erythrocytic activity of superoxide dismutase and catalase. We found significantly elevated plasma MDA level and activity of erythrocytic superoxide dismutase. While plasma total antioxidant capacity and activity of erythrocytic catalase were reduced significantly in SCA patients. These observations provide the evidence of imbalance between oxidant and antioxidant status leading to chronic oxidative stress.

86. Hemoglobin Fontainebleau [a21(B2)Ala>Pro]: The second report from India

2013

Indian Journal of Human Genetics

Mashon, Ranjeet and Nair, Sona and Sawant, Pratibha and Colah, Roshan and Ghosh, Kanjaksha and Das, Sheila

Structural hemoglobin (Hb) variants are mainly due to point mutations in the globin genes resulting in single amino acid substitutions. Until date, about 200 alpha chain variants have been identified and they are usually detected during the hemoglobinopathy screening programs. Under a community control program for hemoglobinopathies, which involved screening of antenatal cases followed by prenatal diagnosis if indicated. Here, we report a rare alpha globin gene variant Hb Fontainebleau [a21(B2)Ala>Pro] detected in the heterozygous condition in a 35-year-old pregnant lady screened during this program. This is the second report of this alpha globin variant from India. Unlike the earlier case from India where Hb Fontainebleau was reported in a neonate who was also a carrier of Hb Sickle and had no clinical problems, this case presented with a bad obstetric history associated with the secondary infertility. However, the presence of the variant and the obstetric complications may be unrelated.

87. **Molecular characterization of [beta]-thalassemia in four communities in South Gujarat--codon 30 (G[arrow right]A) a predominant mutation in the Kachhiya Patel community**

2013

Annals of Hematology

Bhukhanvala, Dipal S and Italia, Khushnooma and Sawant, Pratibha and Colah, Roshan and Ghosh, Kanjaksha and Gupte, Snehalata C

Different thalassemia mutations have been reported in various ethnic groups and geographical regions in India. In this study, we have investigated Kachhiya Patel, Dhodia Patel, Modh Bania, and Muslim communities of Surat, Gujarat to identify molecular defects causing [beta]-thalassemia in them. Covalent reverse dot blot hybridization technique was used to detect six common Indian [beta]-thalassemia mutations while the seventh mutation (619-bp deletion) was identified by PCR. The less common mutations were detected by amplification refractory mutation and the uncharacterized samples were directly sequenced. Characterization of [beta]-thalassemia mutations was carried out in a total of 175 unrelated [beta]-thalassemia trait cases. We identified IVS 1 nt 5 (G[arrow right]C) in 31 out of 65 Muslims, codon (Cd) 41/42 (-CTTT) in 14 out of 16 in Modh Banias, Cd 15 (G[arrow right]A) in 19 out of 24 Dhodia Patels. The most significant observation was an uncommon mutation; Cd 30 (G[arrow right]A) detected in 61 out of 70 Kachhiya Patels. The 619-bp deletion was detected in 6 out of 10 Muslim-Memons. Many other rare mutations like Cd 15 (-T), Cd 8 (-AA), -88 (C[arrow right]A), Capsite +1 (A[arrow right]C), Cd 16(-C), and Cd 5 (-CT) were detected. To our knowledge, our study is the first to characterize [beta]-thalassemia mutations in the Kachhiya Patel community. This study will facilitate molecular analysis and prenatal diagnosis in these four communities.[PUBLICATION ABSTRACT]

88. **Sickle Cell Anemia with Malaria: A Rare Case Report**

2014

Indian Journal of Hematology and Blood Transfusion

Gupta, Narendra Kumar and Gupta, Meenakshi

Sickle cell disease is the prototype of hereditary hemoglobinopathies, characterized by the production of structurally abnormal hemoglobin. Sickle cell anemia results from a point mutation that leads to substitution of valine for glutamic acid at the sixth position of the [beta] globin chain. We report a young male admitted with fever and weakness for 3 days. Hematological test reveals Plasmodium falciparum malaria parasite and sickle cell anemia. Patient was treated and get cured from malaria and discharged.

89. **Rare case of diffuse splenic uptake on methylene diphosphonate bone scan in a patient with sickle cell disease**

2020

Indian Journal of Nuclear Medicine : IJNM

Parida, Girish and Mitra, Sujata and Muthu, Gopal and Suman, Akchata

Extraskeletal tracer uptake in methylene diphosphonate (MDP) bone scan is not a common finding. There have been several case reports in the literature showing diffuse splenic uptake in MDP bone scan. We present a case of sickle cell disease, which showed diffuse splenic uptake on MDP whole-body bone scan.

90. Pseudo-Sickle Anemia: Two Case Reports

2014

Indian Journal of Hematology and Blood Transfusion

Nangia, Anita and Sharma, Sunita and Sethi, Neha and Puri, Vandana and Pujani, Mukta and Beniwal, Anu

Sickle cells in peripheral blood smear are usually seen in sickle cell disease. However in certain very rare conditions, pseudosickle cells may be seen. The present study reports two cases of iron deciency anemia with presence of pseudo sickle cells in the peripheral blood lms which lead to a diagnostic dilemma.

91. Sickle-[beta]^sup +^ thalassemia with splenic calcification and bone marrow infarction: a case report

2008

Indian Journal of Hematology and Blood Transfusion

Kar, Rakhee and Das, Reena and Saxena, Akshay and Chawla, Y and Ahluwalia, Jasmina

We came across an unusual case of a 20 years old male from north India who presented with repeated episodes of pyrexia of unknown origin (PUO) and history of chronic hemolytic anemia. On investigation he was detected to have Sickle-[beta]^sup +^ Thalassemia and subtle features of hyposplenism. Radiological investigations revealed extensive splenic calcification and bone marrow examination to evaluate for PUO showed extensive bone marrow infarction and fibrosis. Molecular diagnosis for beta thalassemia mutation revealed heterozygosity for IVS 1-5 M and alpha globin genes were normal. This case highlights the wide variation of clinical phenotype which is encountered with Sickle-[beta]^sup +^ Thalassemia where genotyping can predict the clinical phenotype only partially.

92. The clinical features of sickle cell disease

1993

Bailliere's Clinical Haematology

Serjeant, G R

Evidence from structural studies of DNA suggest that the sickle cell mutation has arisen on at least three separate occasions in Africa and as a fourth independent mutation in the Eastern Province of Saudi Arabia or India. The pathophysiology of sickle cell disease is essentially similar in these different areas although the frequency and severity of complications may vary between areas. Generally, the chronic haemolysis and resulting anaemia is well tolerated, although serious morbidity and occasionally mortality may be associated with the aplastic crisis or cholelithiasis. Exacerbation of anaemia below steady state levels occurs with chronic glomerular damage and renal failure, especially in older patients. Most of the morbidity of the disease arises from bone marrow necrosis in the painful crisis or from vaso-occlusive manifestations. Changes in the splenic circulation result in life-threatening episodes of acute splenic sequestration, the chronic morbidity of hypersplenism, and splenic dysfunction renders children prone to pneumococcal septicaemia. Chronic organ damage contributes to chronic leg ulceration in adolescence and progressive renal, pulmonary, and occasionally cardiovascular impairment in later life. The clinical spectrum of homozygous sickle cell disease varies widely between patients. Factors contributing to this variability include Î±-thalassaemia, persistence of high HbF levels, haematology, social circumstances, and geographical and climatic variation. Many of the causes of mortality may be prevented or more effectively treated, leading to increased survival and an increased quality of life in affected subjects.

93. Double heterozygous for hemoglobin S and hemoglobin E - A case report from central India
2007

Indian Journal of Hematology and Blood Transfusion

Dani, A A and Shrikhande, A V

Double heterozygosity for HbS and HbE is rare. HbS and HbE are seen in SC, ST and OBC communities from this part of country. Inter caste marriages amongst these communities have resulted into this compound heterozygous condition. Double heterozygous state for HbS and HbE is clinically silent as compared to HbS-Î² Thalassaemia and HbSS cases. At Regional Hemoglobinopathy Detection and Management Center, we report a case of 15-year-old male, Teli (OBC) by caste who came for screening for sickle cell disorder. Sickling, solubility test and Hb electrophoresis on agar gel at alkaline pH was carried out. His sickling and solubility tests were positive and on hemoglobin electrophoresis it showed two bands one at Hb A2 position and another at HbS position. For further confirmation sample was subjected for quantitation of haemoglobin on high performance liquid chromatography (HPLC), Bio-Rad. On quantitation he was having HbS 59.8%, HbE 33.5% and HbF 3.2% confirming his double heterozygous state for HbS and HbE. On family screening his father turned out to be sickle cell trait and mother as hemoglobin E trait. Â© Indian Society of Haematology & Transfusion Medicine 2007.

94. Perinatal outcome in sickle cell anemia: A prospective study from India

2013

Hemoglobin

Daigavane, M M and Jena, R K and Kar, T J

Sickle cell anemia, the homozygous genotype of sickle cell disease is one of the most common heritable diseases in the world. The Arab-Asian haplotype present in India is one of the least severe of all haplotypes. Many sickle cell anemia patients are now leading a symptom-free productive life due to hydroxyurea (HU) and better supportive care. Although pregnancy in sickle cell anemia patients is considered a high-risk category, it perinatal outcome is least studied, particularly among carriers of the Arab-Asian haplotype. Thus, the present prospective, randomized study was performed to assess the perinatal outcome in sickle cell anemia. Neonatal outcome such as low birth weight, perinatal mortality rate, special care newborn unit (SCNU) admission, intrauterine growth retardation (IUGR) and pre term births were significantly higher in sickle cell anemia mothers. Maternal outcome such as severe anemia, preeclampsia, vasoocclusive crisis (VOC), pulmonary complications, jaundice and blood transfusion requirements were significantly higher in sickle cell anemia mothers, which were successfully managed. Cesarian section rate was not significantly different from normal controls. Successful pregnancies were achieved in 84.44% of cases. However, we strongly recommend that pregnancies in these patients should be managed in an institutional setup. Â© Informa Healthcare USA, Inc.

95. Nonrandom association of polymorphic restriction sites in the beta-globin gene cluster.
1982

Proceedings of the National Academy of Sciences of the United States of America

Antonarakis, S E and Boehm, C D and Giardina, P J and Kazazian, H H Jr

By using probes for epsilon-, Psibeta(1)-, and beta-globin genes, we found four additional polymorphic restriction sites that have frequencies >0.1 in persons of Mediterranean area origin, Asian Indians, and American Blacks. Three of these (HincII sites) and the two previously described polymorphic HindIII sites [one in intervening sequence (IVS) II of each gamma-globin gene] are distributed over 32 kilobases (kb) of DNA located 5' to the delta-globin gene. This region of DNA comprises two-thirds of the beta-globin gene cluster. Since each of these five polymorphic sites can be present (+) or absent (-), in theory there exist 32 possible combinations of sites (haplotypes). However, in Italians, Greeks, Indians, and Turks, 3 of the 32 haplotypes, (+----), (-+-++), and (-++-

+), account for 92% of 89 beta(A) chromosomes examined. The observed frequencies for these haplotypes are 0.64, 0.15, and 0.13 in the populations studied, in contrast to expected frequencies (based on the observed gene frequencies at each of the five sites) of 0.20, 0.006, and 0.005, respectively. In American Blacks, a fourth haplotype, (----+), which is rare in non-Black populations, has a frequency of 0.37 in contrast to its expected frequency of 0.05. These results suggest a nonrandom association of DNA sequences over 32 kb 5' to the delta-globin gene in all populations studied. Two other polymorphic sites 3' to the delta gene (the newly discovered Ava II site in IVS II of the beta-globin gene and the BamHI site 3' to it) are nonrandomly associated with each other but randomly distributed with respect to the above haplotypes. This suggests that randomization of sequences has occurred within 12 kb of DNA between these two nonrandomly associated sequence clusters. Nonrandom association of polymorphic restriction sites has practical consequences in that it limits the usefulness of these additional HincII sites for prenatal diagnosis of hemoglobinopathies by linkage analysis. These sites provide little additional information for detection of beta-thalassemia, while the polymorphic Ava II site, which lies outside the nonrandomly associated sequences 5' to the delta gene, improves the test applicability from 52% to 70% of couples at risk.

96. NAT2 genetic variations among South Indian populations.

2014

Human genome variation

Lakkakula, Saikrishna and Mohan Pathapati, Ram and Chaubey, Gyaneshwer and Munirajan, Arasambattu Kannan and Lakkakula, Bhaskar Vks and Maram, Rajasekhar

The N-acetyltransferases (NATs) are xenobiotic-metabolizing enzymes involved in the metabolism of drugs, environmental toxins and the aromatic amine carcinogens present in cigarette smoke. Genetic variations in NAT2 have long been recognized as the cause of variable enzymatic activity or stability, leading to slow or rapid acetylation. In the present study, we genotyped three single-nucleotide polymorphisms (SNPs) from the NAT2 gene (rs1799929, rs1799930 and rs1799931), using TaqMan allelic discrimination, among 212 individuals from six major South Indian populations and compared the results with other available Indian and worldwide data. All three of the markers followed Hardy-Weinberg equilibrium and were highly polymorphic in the studied populations. The constructed haplotypes showed a high level of heterozygosity. All of the populations in the present study commonly shared only four haplotypes out of the eight possible three-site haplotypes. The haplotypes exhibited fairly high frequencies across multiple populations, where three haplotypes were shared by all six populations with a cumulative frequency ranging from 88.2% (Madiga) to 97.0% (Balija). We also observed a tribal-specific haplotype. A strong linkage disequilibrium (LD) between rs1799929 and rs1799930 was consistent in all of the studied populations, with the exception of the Madiga. A comparison of the genomic regions 20-kb up- and downstream of rs1799930 in a large number of worldwide samples showed a strong LD of this SNP with another NAT2 SNP, rs1112005, among the majority of the populations. Moreover, our lifestyle test (hunter-gatherer versus agriculturist) in comparison with the NAT2 variant suggested that two of the studied populations (Balija and Madiga) have likely shifted their diet more recently.

97. HbQ-India in a Sindhi family: an uncommon hemoglobin variant.

2004

Laboratory hematology : official publication of the International Society for Laboratory Hematology

Desai, Devenkumar V and Dhanani, Hiren and Kapoor, Amit K and Yeluri, Sashidhar V

Hemoglobin Q-India is a very rare alpha-chain structural variant caused by the mutation AAG-->GAG (Asp-->His) in the position of codon 64 of the alpha1 gene. Usually it presents in the heterozygous form with electrophoretic mobility in the position of hemoglobin S (HbS) at alkaline pH along with the double bands of HbA2. High-performance liquid chromatography (HPLC) retention time of 4.76 minutes for this abnormal Hb

variant identifies it to be HbQ-India. Only isolated case reports exist in literature to describe this rare entity. On cellulose acetate electrophoresis at alkaline pH, the HbQ band can easily be misinterpreted as HbS or HbD if careful screening of the patient for sickle cell with solubility test or sickling test is not done and the abnormal HbA2 band is overlooked. We report a case and emphasize the importance of careful screening with electrophoresis and HPLC in the diagnosis of this rare condition

98. Clinical variability and molecular characterization of Hbs/GÎ³ (AÎ³Î´Î²)0-thal and Hbs/HPFH in Indian sickle cell disease patients: AIIMS experience

2019

Hematology (United Kingdom)

Pandey, H and Singh, K and Ranjan, R and Pandey, S K and Sharma, A and Kishor, K and Seth, T and Mahapatra, M and Saxena, R

Introduction: In sickle cell disease (SCD) patients, among the predictors of survival, HbF levels play a significant role in lowering the morbidity and mortality. Coinheritance of Î´Î² thalassemia and hereditary persistence of fetal hemoglobin (HPFH) may contribute to variable HbF levels in SCD patients, thus influencing their clinicopathological profile. Such cases are sparsely documented in the literature and thus, we screened the presence of Î´Î² thalassemia and HPFH in 126 cases of SCD with high HbF. Material and methods: A total 126 SCD individuals with raised HbF levels were the study subject. Capillary zone electrophoresis (CZE) was done for the quantitative assessment of hemoglobin variants. HbSC, HbSD, HbAS and HbSE cases were excluded. Asian Indian GÎ³(AÎ³Î´Î²)0-thal, Î´Î²0-thal (Sicilian, 13.4 kb), (Chinese, 100 kb), HPFH-1 (Black, 106 kb), HPFH-2 (Ghanaian, 105 kb), HPFH-3 (Indian, 48.5 kb) were done by GAP-PCR. Results: Out of 126, 78 cases (62%) were homozygous for SCD. The remaining 48 cases suspected to be heterozygous were furthered screened and 6/48 cases (12.5%) were found to be compound heterozygous. Out of these 6 cases,4(66.66%) had HbS/ Î´Î²-GÎ³(AÎ³Î´Î²)0 and 2(33%) had HbS/HPFH compound heterozygous condition. None of the patients had Î´Î²0-thal (Sicilian, 13.4 kb), (Chinese, 100 kb), HPFH-1 (Black, 106 kb), HPFH-2 (Ghanaian, 105 kb). Conclusion: This study highlights the importance of understanding the complex patho-physiology of compound heterozygous cases of HbS/HPFH and HbS/Î´Î² thalassemia, as these infrequent conditions lead to change in phenotype and clinical severity of the disease. Insight into more such cases will open the window to better analyze the disease pathogenesis in these rare compound heterozygous conditions, as this will be beneficial to formulate proper management protocol in these patients.

99. Clinical, genetic and fertility studies of Indians with beta S-globin gene and the influence of Hb S on Plasmodium falciparum malaria infection.

1988

Transactions of the Royal Society of Tropical Medicine and Hygiene

Joishy, S K and Hassan, K and Lopes, M and Lie-Injo, L E

Clinical studies were carried out on mild Indian sickle cell anaemia in Malaysia, and genetic and fertility studies were carried out on 101 families with and without sickle-cell haemoglobin (Hb S). The Indian sickle cell anaemia patients reached adulthood, and pregnancies and deliveries were uneventful without blood transfusion. There was no foetal wastage and the number of children produced was not significantly different from that in families without Hb S. 28 Indian patients hospitalized with Plasmodium falciparum malaria infection were also examined for their beta S genotype. P. falciparum malaria infection occurred much more frequently in individuals without Hb S than in Hb S carriers.

100. Clinical, hematologic and molecular variability of sickle cell-Î² thalassemia in western India

2010

Indian Journal of Human Genetics

Mukherjee, M B and Nadkarni, A H and Gorakshakar, A C and Ghosh, K and Mohanty, D and Colah, R B

Background: Sickle cell-thalassemia (HbS-Î² thalassemia) is a sickling disorder of varying severity, which results from compound heterozygosity for sickle cell trait and thalassemia trait. The present study was undertaken to determine the genetic factors responsible for the clinical variability of HbS-Î² thalassemia patients from western India. Materials and Methods: Twenty-one HbS-Î² thalassemia cases with variable clinical manifestations were investigated. The and globin gene clusters were studied by molecular analysis. Results: Thirteen patients showed milder clinical presentation as against eight patients who had severe clinical manifestations. Four Î² thalassemia mutations were identified: IVS 1-5 (Gâ†'C), codon 15 (Gâ†'A), codon 30 (Gâ†'C) and codon 8/9 (+G)Î± thalassemia and XmnI polymorphism in homozygous condition (+/+) were found to be common among the milder cases. The Î²S chromosomes were linked to the typical Arab-Indian haplotype (#31). Framework (FW) linkage studies showed that four Î² thalassemia mutations were associated with different Î² globin gene frameworks. Linkage of codon 15 (Gâ†'A) mutation to FW2 is being observed for the first time. Conclusion: The phenotypic expression of HbS-Î² thalassemia is not uniformly mild and thalassemia and XmnI polymorphism in homozygous condition (+/+) are additional genetic factors modulating the severity of the disease in the Indian subcontinent.

101. A positive correlation between sickle cell anemia and g6pd deficiency from population of Chhattisgarh, India

2019

Gene

Shivwanshi, L R and Singh, E and Kumar, A

Objective: Present study was undertaken to study the association between sickle cell anemia (SCA)and glucose-6-phosphate dehydrogenase (G6PD)deficiency from Sahu and Kurmi population of Durg and Rajnandgaon district of Chhattisgarh, India. Method: A random sampling of 1749 individuals was done. SCA and G6PD deficiency was detected by slide test followed by electrophoresis and Enzymatic reaction indicated by change in colour respectively. Further the samples were subjected to analyze glutathione-S-transferase (GST)i.e. GSTM1 and GSTT1 gene polymorphism, variance of G6PD among G6PD deficient samples by PCR-RFLP. Oxidative stress and DNA damage by comet assay was also analyzed. Results: Present finding indicates positive correlation between SCA and G6PD deficiency in Durg and Rajnandgaon district [Durg: (r = 0.92; HbAS-G6PDd and r = 0.56; HbSS-G6PDd)Rajnandgaon: (r = 0.63; HbAS-G6PDd and r = 0.86; HbSS-G6PDd)]. Significant changes (P < 0.05)in antioxidant enzymatic parameters were observed in HbSS and G6PD with sickle positive individual. Assessment of DNA damage by Comet assay considering Head DNA percent, Tail DNA percent, Tail length and Tail moment also showed significant changes (P < 0.05)within all concerned parameters in HbSS and G6PD with sickle positive individual. Analysis of GST gene polymorphism showed that frequency of individuals carrying the GSTM1 null genotype was higher in HbAS (60%)and the frequency of individual carrying the GSTT1 null genotype was found higher in HbSS (66.6%). G6PD variants analysis also confirmed the presence of highest percentage of mutation among G6PD deficient population as compared to control and a positive correlation was observed between G6PD deficiency and mutant variants of G6PD gene [Rajnandgaon: (r = 0.67; G6PDd-Mahidol mutated and r = 0.90; G6PDd-Union mutated)Durg: (r = 0.91; G6PDd-Mahidol mutated and r = 0.01; G6PDd-Union mutated)]. Conclusion: Thus present finding indicates positive correlation between SCA and G6PD deficiency in Chhattisgarh, India.

102. Association of DNA damage repair gene polymorphisms hOGG1, XRCC1and p53 with sickle cell disease patients in India

2015

Mediterranean Journal of Hematology and Infectious Diseases

Nishank, S S

Background: Oxidative stress constitutes one of the significant cause of vaso-occlusive clinical episodes in sickle cell disease (SCD) patients. It brings about the generation of reactive oxygen species and consequent damage to DNA. DNA damage repair genes such as hOGG1, XRCC1 and p53 play an important role in the repair of DNA damage during oxidative stress. However, it is not known as to the role of these genes in oxidative stress mediated vaso-occlusive clinical complications of SCD patients. Objective: To see the possible association of DNA repair gene polymorphisms with clinical manifestation of SCD patients. Methods: Genotyping of DNA damage repair genes by PCR-RFLP, measurement of oxidant and anti-oxidant status, along with a clinical evaluation of 250 SCD patients and their comparison with normal individuals. Result: The level of oxidants were high, and that of antioxidants were low in SCD patients compared to normal individuals. The prevalence of mutant alleles of hOGG1 gene, XRCC1 gene (codon 280 Arg>His) were found to be significantly higher among SCD patients as compared to controls. However, SCD patients did not show clinical association with any of these DNA repair gene polymorphisms. Conclusion: This indicates that hOGG1, p53and XRCC1 gene polymorphisms have no clinical association with SCD patients in India.

103. Mutation -538 T/C in bone morphogenetic protein 4 do not increase the risk in sickle-cell disease with orthopedic complications but strongly associated with increased LDH and uric acid level in Indian patients from Chhattisgarh and Jharkhand states

2010

Clinica Chimica Acta

Abhishek, K and Sohail, M and Kumar, R and Patra, P K and Choudhary, S B

Background: Bone morphogenetic protein (BMP) are involved in the various orthopedic complications such as avascular necrosis, osteonecrosis and bone turnover, therefore genes coding for proteins, like BMP4, can be potential candidate for studying orthopedic disorders. Methods: A case-control study was conducted to examine the association between SNP T538C of BMP4 and orthopedic complications in sickling patients by employing PCR-RFLP. Results: A total of 200 cases and 172 control groups were studied from Indian population. T538C SNP has not been implicated in disease and doesn't increase the risk (OR=0.89, OR=0.68). We observed no significant association between the T538C polymorphism and case group in the studied population. However, we observed significantly increased uric acid and LDH level in homowild (TT), heteromutant (TC) and homomutant (CC) in case group compared to control group (all p=0.0001) and (p=0.0001, p=0.0001, p=0.015 and p=0.0001, p=0.0001, p=0.0001 respectively) in the studied population. Conclusions: The T/C polymorphism in BMP4 is not associated with case group and in view of present observation, we suggest that evaluation of LDH and uric acid level and its association with polymorphisms in the BMP4 may be considered to be reliable molecular and biochemical markers, and possess promising rational for diagnostic potential in clinical cases. Â© 2010 Elsevier B.V.

104. Effect of ANXA2 gene single nucleotide polymorphism (SNP) on the development of osteonecrosis in Indian sickle cell patient: A PCR-RFLP approach

2012

Indian Journal of Experimental Biology

Pandey, S and Ranjan, R and Pandey, S and Mishra, R M and Seth, T and Saxena, R

Osteonecrosis is a serious complication in sickle cell patients. The common sites of the necrosis are femoral head, head of the humerus and acetabulam. Annexin A2 (ANXA2) protein mainly functions in bone formation and bone resorption. Alteration of ANXA2 gene may affect the manifestations of osteonecrosis in the patients. PCR-RFLP is a common applicable technique for the detection of known mutation/polymorphisms. Here we are presenting application of the PCR-RFLP technique for determination of the ANXA2 gene single nucleotide polymorphism frequency and their clinical association among Indian sickle cell patients. Five known SNPs of ANXA2 gene (rs7170178, rs73435133, rs73418020, rs72746635 and rs73418025) were determined using the HpyCH4V, DdeI, HpyCH4III and Sau 961 restriction enzyme respectively. Restriction enzyme DdeI was common for rs73435133 and rs72746635 SNP. Only the rs7170178 SNP was detected among patient and control and the other four SNPs were absent in the studied groups. The frequency of ANXA2 gene rs7170178 SNP (A/G, G/G) was comparatively higher in sickle cell patients than controls and it was clinically associated with sickle cell osteonecrosis. The P value of heterozygotes (A/G) and homozygotes (G/G) genotypes were <0.001 and 0.001 respectively, which were highly significant. This study established the application of PCR-RFLP in detection of ANXA2 SNPs in sickle cell patients.

105. Clinical profile of sickle cell trait.

2002

The Journal of the Association of Physicians of India

Kar, B C

OBJECTIVES: Although sickle cell trait is considered a harmless condition in ordinary circumstances, a large number of pathological conditions have been attributed to it often without a scientific basis. Many patients visit this centre with various complaints and on testing are found to be sickle cell trait. Hence it was thought necessary to analyse these cases to find out the nature of their ailments. METHODS: Two hundred cases of sickle cell trait diagnosed by sickling test and hemoglobin electrophoresis on CAM, and 150 age and sex matched control cases with normal hemoglobin phenotype from a survey were studied. Hemoglobin estimation was done in all by cyanmethemoglobin method. Besides history and clinical examination other relevant investigations were done as necessary to arrive at the diagnosis. Seven cases of sickle cell trait were asymptomatic while the rest were suffering from different conditions. 51% of sickle cell trait and 86% of control cases had mild to severe anaemia which improved with iron therapy in trait cases. Hepatomegaly (11% vs 4.6%), epistaxis (5% vs 0.66%) and cholelithiasis (3% vs 0%) was seen in significantly more number in sickle cell traits than the control cases. Splenomegaly and midsystolic murmurs were present in higher percent of cases but was not statistically significant. There was one case of epilepsy with multiple small infarcts in the brain and another with focal fits with epileptogenic focus in the left cerebral hemisphere where no other cause could be found except sickle cell trait. CONCLUSION: The ailments of sickle cell trait cases are like persons with normal hemoglobin. Anaemia is not more frequent and can improve with iron therapy. However, hepatomegaly, epistaxis, cholelythiasis are seen more frequently and minor cerebral infarcts probably can occur in sickle cell trait. These require more elaborate studies to decide their pathogensis.

106. Is hemoglobin E gene widely spread in the state of Madhya Pradesh in central India? Evidence from five typical families

2014

Mediterranean Journal of Hematology and Infectious Diseases

Balgir, R S

Background: Red cell inherited hemoglobin (Hb) anomalies are commonly encountered in the central region of India. These cause a public health concern due to high level of morbidity, mortality, and fetal loss in the backward, underprivileged, and vulnerable people. Purpose: To report five typical families of Hb E disorders for the first time detected and identified from various districts of the state of Madhya Pradesh in central India. Methods: Out

of a total of 447 couples/families referred from a tertiary hospital in central India for investigations of anemia/hemoglobinopathies during the period from March 2010 to February 2014, we came across five typical rare couples/families of Hb E disorders (1.1%) worthy of detailed investigations that we have reported here. Laboratory investigations were carried out following the standard procedures after cross checking for quality control from time to time. Results: For the first time, out of total 27 cases studied, we have encountered nine cases of heterozygous Hb E trait (33.3%), two members (7.4%) with Hb E-ÃŸ-thalassemia (double heterozygosity), two cases (7.4%) of sickle cell-Hb E disease (double heterozygosity), two ÃŸ-thalassemia traits (7.4%), three sickle cell traits (11.1%), 9 normal (33.3%), and none with homozygous Hb E disease. Cases of Hb E trait, Hb E-ÃŸ-thalassemia, and sickle cell-E disease showed moderate to severe anemia, and target cells, and reduced values of red cell indices like red blood cell count, Hb level, hematocrit, mean cell volume, mean cell Hb and mean cell Hb cencentration, describing abnormal hematological profile and clinical manifestations before blood transfusion. Conclusions: Double heterozygosity of ÃŸ-thalassemia with Hb S and Hb E is a rare entity, but occurs with severe clinical manifestations, testifying either migrations and/or genetic admixture. Co-occurrence of Hb E/ÃŸ-thalassemia in different districts indicates that these anomalies along with other hemoglobinopathies are wide spread in Madhya Pradesh and posing a major genetic burden on vulnerable people of central India.

107. Association of low serum iron with alpha globin gene deletions and high level of HbF with Xmn-1 polymorphism in sickle cell traits

2012

Indian Journal of Clinical Biochemistry

Pandey, S and Mishra, R M and Suhail, A and Rahul, S and Ravi, K and Pandey, S W and Seth, T and Saxena, R

Usually sickle cell traits are asymptomatic but co-existence of various factrors may alter the clinical as well as biochemical levels. In India sickle cell traits are neglected condition. Here we are presenting the alpha deletion in association with low serum iron and increased HbF level with Xmn-1 carriers in sickle cell traits. Sickle traits with alpha deletions had significantly low level of serum iron (P-value < 0.05) with low level of reticulocytes and red cell indices while Xmn-1 polymorphism associated with increased HbF level. Study concludes low serum iron associated with alpha deletions and high level of HbF associated with Xmn-1 polymorphism in sickle cell traits. Â© Association of Clinical Biochemists of India 2012.

108. Genetic distances among the Ho tribe and other groups of Central Indians.

1975

American journal of physical anthropology

Kumar, N and Mukherjee, D P

The Ho, a settled tribal group of Chota Nagpur, India, were tested for five genetic characters. Genetic distance among eleven tribal groups of Bihar, Orissa and Madhya Pradesh are calculated according to Edwards ('71). Affinities of these tribes are discussed taking into consideration the languages spoken by them. These breeding groups may have drifted apart along the paths of their dialect differentiations. Cultural and geographical factors further enhanced their isolation.

109. Haemoglobin s interaction with Beta thalassaemia- a case report from assam, India.

2014

Journal of clinical and diagnostic research : JCDR

Pathak, Mauchumi Saikia and Borah, Monalisha Saikia and Kalita, Dulal

Interaction of Hb S with beta thalassaemia is being reported here as this type of case is rare. Hb S (Î²6 gluâ†'val) is a genetic disorder which occurs due to beta globin gene mutation of haemoglobin. In India, the Hb S is prevalent in the central part, in the eastern, western and southern tribal belt regions and among the tea tribe communities of Assam. The Hb S carriers (Sickle cell trait) leads a normal life but the Sickle cell disease patients show certain clinical manifestation like joint pain, anaemia and jaundice. The HPLC report of the patient showed Compound heterozygous for Hb S- Î² thalassaemia. The complete blood count was measured in automated haematology analyser. Mutational pattern of the beta thalassaemia as well as the presence of Hb S gene was detected by PCR. The case showed severe clinical manifestations and transfusion was required due to inheritance of the IVS 1-5 G â†'C Î²- thalassaemia mutation with the Hb S gene.

110. Endothelial nitric oxide synthase (eNOS) gene polymorphism is associated with age onset of menarche in sickle cell disease females of India

2013

Mediterranean Journal of Hematology and Infectious Diseases

Nishank, S S

Background and Objective: Females with sickle cell disease (SCD) often show late onset of menarche. In transgenic sickle cell mouse, deficiency of gene encoding endothelial nitric oxide synthase (eNOS) has been reported to be associated with late onset of menarche. Thus to explore the possible association of eNOS gene polymorphism with age of onset of menarche in SCD females, 3 important eNOS gene polymorphisms- eNOS 4a/b, eNOS 894G>T (rs1799983) and eNOS-786 T>C (rs2070744) and plasma nitrite levels were tested among three groups of females- SCD late menarche, SCD early menarche and control females. Methodology: About 39 SCD females comprising of 18 SCD early menarche and 21 SCD late menarche groups were studied along with 48 control females. Genotyping of eNOS gene polymorphisms were done by PCR-RFLP and quantification of plasma nitrite level was performed by ELISA based commercial kits. Results: SCD late menarche females showed significantly higher prevalence and higher association of heterozygous genotypes, higher frequency of mutant alleles '4a', 'T' and 'C' as compared to that of control group and SCD early menarche group. The frequency of haplotype '4a-G-C' and haplotype '4b-G-C' (alleles in order of eNOS 4a/b, eNOS 894G>T and eNOS-786 T>C respectively) were found to be significantly high in SCD late menarche compared to combined groups of SCD early menarche and controls. SCD late menarche group had significantly low level of plasma nitrite concentration for all 3 eNOS gene polymorphisms as compared to controls and SCD early menarche females. Conclusion: eNOS gene polymorphism may influence age of onset of menarche in SCD females.

111. Generation and characterization of induced pluripotent stem cell line (IGIBi001-A) from a sickle cell anemia patient with homozygous Î²-globin mutation

2019

Stem Cell Research

Bhargava, N and Jaitly, S and Goswami, S G and Jain, S and Chakraborty, D and Ramalingam, S

Sickle cell disease (SCD) is an autosomal recessive disorder caused by a mutation in Î²-globin (HBB) gene. We have generated an induced pluripotent stem cell (iPSC) line, IGIBi001-A from an Indian sickle cell patient with a homozygous HBB gene mutation using Sendai virus reprogramming system. Characterization of IGIBi001-A showed that these iPSCs are transgene-free and expressed pluripotent stem cell markers. They had a normal karyotype and were able to differentiate into all three germ layers. This new SCD-iPSC line will contribute to better understanding of the disease biology of sickle cell anemia and for screening of small molecule drugs.

112. Interaction of -Î± 3.7, Î² thalassemia mutation IVS 1-5 and HbD Punjab in a family: A case report

2012

Indian Journal of Clinical Biochemistry

Pandey, S and Ranjan, R and Mishra, R M and Pandey, S W and Saxena, R

Hemoglobin D exist in four form; HbD trait, HbD-thalassemia, HbD sickle cell and HbD homozygous. HbD trait and HbD homozygous generally asymptomatic condition but when HbD co-inherit with thalassemia and sickle cell anemia, produces clinically significant conditions like chronic hemolytic anemia. Here we present a case of HbD Punjab with Î± 3.7 kb deletion and IVS-1-5 Î²-thalassemia across a family. Diagnosis of HbD patient was performed by high performance liquid chromatography and complete blood count was measured by automated cell analyzer. Molecular study for common alpha deletions done by Gap-PCR while beta thalassemia mutation identified by ARMS-PCR. Case was clinically significant due to the inheritance of HbD/Î² +thalassemia genotype. Thus observed case behaved like thalassemia intermedia due to co-existence of Î± 3.7 deletions with IVS 1-5 Î²-thalassemia mutation in HbD Punjab patient. Â© Association of Clinical Biochemists of India 2012.

113. Comparative study of alloimmunization against red cell antigens in sickle cell disease & thalassaemia major patients on regular red cell transfusion

2019

Indian Journal of Medical Research

Jariwala, K and Mishra, K and Ghosh, K

Background & objectives: Sickle cell disease (SCD) patients require red cell transfusion during different clinical complications of the disease. Such patients are at a high risk for developing alloantibody against red cell antigens. From India, there are limited data available on alloantibody formation in multiply transfused SCD patients. The present study was thus undertaken to fill up this lacunae by looking at the development of red cell alloantibodies in SCD and Î²-thalassaemia patients on regular transfusion. Methods: All sickle cell disease patients undergoing red cell transfusion between 2008 and 2016, were included. During this period, a large number of Î²-thalassaemia major patients also underwent regular red cell transfusion. These thalassaemia patients were also included to compare the tendency of antibody formation between SCD and Î²-thalassaemia major patients. All patients before regular transfusion were regularly assessed for the development of red cell antibody. Red cell antigen, antibody screen crossmatch and antibody identification were done using the standard technique. Results: A total of 138 patients with SCD aged between 4 and 53 yr (mean 17.6 yr) consisting of 83 males and 55 females (male:female, 1.5:1) along with 333 transfusion-dependent Î²-thalassaemia patients were studied. Over the last eight years, 15 patients with SCD and four patients with thalassaemia developed alloantibody (P <0.001). Antibody specificity of their alloantibodies was against Rhc, RhE, Kell, Fya and Fyb only. Sickle cell disease patients with and without alloantibody required on the average 11.8 and 8.6 units of red cell concentrate, respectively (P <0.05). Interpretation & conclusions: About 11 per cent of the transfused sickle cells patients developed alloantibodies. The antibody specificity was restricted to Rh, Kell and Duffy blood group systems. Extended antigen matching involving Rh, Kell and Duffy antigens may prevent alloantibody in such patients.

114. An anthropometric and hematological comparison of sickle cell disease children from rural and urban areas

2012

Indian Journal of Human Genetics

Nikhar, H S and Meshram, S U and Shinde, G B

Background: Sickle cell disease (SCD) is a prevalent genetic disorder in India and the rural and urban areas experience distinctly different healthcare facilities. In view of this, a comparative study of SCD-SS pattern children of age 8-15 years from rural and urban areas of Wardha district of Central India was carried out using anthropometric and hematological parameters. Materials and Methods: The data were collected using standard methods and the results showed a significant ($P < 0.05$) difference in the mean values for body weight, body mass index (BMI), hemoglobin, hematocrit, and white blood corpuscles (WBC). Statistical analysis of the data was done using SPSS 18.0 software. Individuals were screened by solubility test method. Sickle cell patterns (AS and SS) were determined by using electrophoresis technique. Result : The SCD-SS children from rural were significantly underweight than those from the urban area of Wardha district. BMI is a good indicator of nutritional status and BMI values of SCD children have less than desired. Conclusion : The study highlights an urgent need to conduct integrated investigations for SCD population of rural areas covering clinical, nutritional, and social aspects.

115. Endothelial nitric oxide synthase gene polymorphism is associated with sickle cell disease patients in India

2013

Journal of Human Genetics

Nishank, S S and Singh, M.P.S.S. and Yadav, R and Gupta, R B and Gadge, V S and Gwal, A

Patients with sickle cell disease (SCD) produce significantly low levels of plasma nitric oxide (NO) during acute vaso-occlusive crisis. In transgenic sickle cell mice, NO synthesized by endothelial nitric oxide synthase (eNOS) enzyme of vascular endothelial cells has been found to protect the mice from vaso-occlusive events. Therefore, the present study aims to explore possible association of eNOS gene polymorphism as a potential genetic modifier in SCD patients. A case control study involving 150 SCD patients and age- and ethnicity-matched 150 healthy controls were genotyped by PCR-restriction fragment length polymorphism techniques for three important eNOS gene polymorphisms - eNOS 4a/b, eNOS 894G>T and eNOS -786T>C. It was observed that SCD patients had significantly higher frequencies of mutant alleles besides heterozygous and homozygous mutant genotypes of these three eNOS gene polymorphisms and low levels of plasma nitrite (NO 2) as compared with control groups. The SCD severe group had significantly lower levels of plasma NO 2 and higher frequencies of mutant alleles of these three SNPs of eNOS gene in contrast to the SCD mild group of patients. Haplotype analysis revealed that frequencies of one mutant haplotype '4a-T-C' (alleles in order of eNOS 4a/b, eNOS 894G>T and eNOS -786T>C) were significantly high in the severe SCD patients ($P<0.0001$), whereas the frequency of a wild haplotype '4b-G-T' was found to be significantly high ($P<0.0001$) in the SCD mild patients, which indicates that eNOS gene polymorphisms are associated with SCD patients in India and may act as a genetic modifier of the phenotypic variation of SCD patients.

116. Hematological parameters and RBC TBARS level of Q 10 supplemented tribal sickle cell patients: A hospital based study

2013

Indian Journal of Clinical Biochemistry

Thakur, A S and Littaru, G P and Moesgaard, S and Dan Sindberg, C and Khan, Y and Singh, C M

The study has been undertaken as number of sickle cell patients in Chhattisgarh tribal population is 23.7 %. The Co enzyme Q10 is a strong antioxidant and energy producing compound. The patients were divided into three groups group A homozygous (SS), group B heterozygous (AS) and group C controls for TBARS study. The age group is 10-55 years and 200 mg of CoQ10 was given to A and B groups. The hematological parameters, C reactive protein as well as RBC TBARS level were performed by usual and standard techniques. The results were obtained as 25.37 % increased RBC level in group A and 23.24 % in group B. The increased hemoglobin level

was observed as 16.73 % in group A and 10.7 % in group B. In case of WBC it was observed increased 24.38 % in group A and 12.0 % in group B. C-reactive protein was observed 7.8 times decreased in group A and 1.54 times in group B. The RBC TBARS level was also found decreased 48 % in group A and 51 % in group B as compared to group C. During the supplementation of coenzyme Q10 the pain caused by vaso-occlusive events has reduced. This significant increase in hematological parameters as well as decreased C-reactive protein and TBARS level suggest that the Q10 should be included in the diet of sickle cell patients. Â© 2012 Association of Clinical Biochemists of India.

117. Mutational analysis of thalassemia in transfusion-dependent beta-thalassemia patients from central India.

2019

Asian Journal of Transfusion Science

Shrivastava, Manisha and Bathri, Rashmi and Chatterjee, Nirupama

BACKGROUND: Thalassemia and hemoglobin (Hb) disorders are the most common genetic disorders among humans. These disorders entail huge morbidity, economic, and psychological burden on the families of the affected. Genetic counseling and prenatal diagnosis are the steps, which helps to reduce this burden. At present, there is paucity of data on the mutational spectrum of thalassemia from the central Indian region. METHODS: Blood samples were collected from 62 transfusion-dependent patients, demographic and relevant data were collected and screened for the two rare mutations âˆ’ 88 (C-T) and CAP + 1 (A-G) using amplification refractory mutation system-polymerase chain reaction (PCR) and GAP PCR technique. PCR was performed for rare Hb disorders such as Hb Lepore and Î´ Î² chain disorder by GAP PCR in addition to five common Indian beta-thalassemia mutations IVS1-5 (G-C), IVS1-1 (G-T), Cd41/42 (âˆ’TCTT), Cd8/9 (+G), 619 bp deletion. RESULTS: Overall 93.5% of the mutations could be identified. Among the abnormal Hb, sickle cell and HbE were found at 4% and 3% of all the loci studied. We also reported two loci with Hb Î´ Î² and one locus with Hb Lepore in the present samples. IVS I-5 (Gâ€“C) was the common mutation (46%) followed by IVS I-1 (Gâ€“T) (12%) and 619 bp (9%). CONCLUSION: The identification of the genotypes helps to define the severity of the phenotype, plan therapy and form the basis of the comprehensive diagnostic database that would be useful not only for genetic counseling but prenatal diagnosis as well, contributing to the current focus of the National Policy to prevent and control hemoglobinopathies.

118. A case of delayed hemolytic transfusion reaction in sickle cell disease patient.

2016

Asian Journal of Transfusion Science

Dogra, Ashu and Sidhu, Meena

Sickle cell disease (SCD) is autosomal recessive, genetically transmitted hemoglobinopathy responsible for considerable morbidity and mortality. It is prevalent in many parts of India including Central India, where the prevalence in different communities has ranged from 9.4% to 22%. Perioperative management may include transfusion of red blood cells. Hemolytic transfusion reactions can occur, and these can be either acute or delayed. We present a case of delayed hemolytic transfusion reaction in a patient with SCD.

119. Descriptive profile of Î²-thalassemia mutations in West Bengal population: a hospital-based study.

2014

International Journal of Hematology

Bhattacharyya, Deboshree M and Mukhopadhyay, Ashis and Basak, Jayasri

The present study was based in a hospital at which 660 individuals have been screened for thalassemia in the past 4 years. The main purposes of the study were to identify different types of beta mutations prevailing among these patients, and to establish a genotype-phenotypic correlation. Complete blood count, high-performance liquid chromatography, and amplification refractory mutation system-based polymerase chain reaction were performed on peripheral blood samples to detect beta mutations. Of the 660 subjects studied, 380 (57.6 %) were male and 280 (42.4 %) were female. These included 258 (39.09 %) normal individuals, 176 (26.67 %) Î²-thalassemia carriers, 44 (6.67 %) Î²-thalassemia major, 6 (0.91 %) cases of sickle Î²-thalassemia, 6 (0.91 %) carriers of sickle cell anemia, 102 (15.45 %) Hb EÎ²-thalassemia, 42 (6.36 %) HbE carriers, 16 (2.42 %) HbE homozygous, and 10 (1.52 %) carriers of other mutations. Genotypic study of beta mutations revealed the prevalence of IVS1-5 mutation among the studied beta carriers to be 46.6 %, and codon 26 (G>A) mutation to be 31.54 %. Other prevailing mutations among the screened individuals include codon 30 (7.53 %), codon 15 (5.01 %), codon 41/42 (3.58 %), and codon 8/9 (1.07 %). Genotype-phenotype correlation revealed that the phenotype of the above-mentioned mutations is associated with mild, moderate, and severe forms of thalassemia.

120. Transfusion in sickle cell disease: experience from a Gujarat centre.

2014

Indian Journal of Pediatrics

Mehta, Vishal and Mistry, Abhishek and Raicha, Bhavesh and Italia, Yazdi and Serjeant, Graham

Objectives: Following impressions that the use of blood transfusion in sickle cell disease may be inappropriately high, transfusion practice at a major blood bank in an area of high prevalence of sickle cell disease was assessed.Methods: Retrospective review of blood usage in sickle cell disease at a major blood bank in south Gujarat in 2010 was conducted with prospective more detailed data collection over 18Â wk period (April 7 through August 15) in 2011. The results were compared with transfusion usage in the Jamaican Sickle Cell Clinic.Results: In 2010, this blood bank processed a total of 19,037 units of which 384 (5.2Â %) units were for patients with sickle cell disease. Median transfusion use was 1 unit but 16 patients (4.2Â %) of those transfused received 10 units or more and five patients received over 20 units. More detailed prospective analysis revealed that most transfusions occurred between ages 5-15Â y, 40Â % of subjects had pretransfusion hemoglobin levels below 6Â g/dL, symptoms were generally vague such as fever, bone pain, weakness and that 26Â % denied any specific symptoms.Conclusions: Transfusion usage greatly exceeds that in the Jamaican Sickle Cell Clinic. Transfusion therapy carries risks and cost and more detailed investigation and diagnosis of anemic episodes is necessary to define the role of transfusion among other potential therapies. Eventually, guidelines evolved by Indian specialists should determine the indications for transfusion in sickle cell disease.

121. Comprehensive integrated care for patients with sickle cell disease in a remote aboriginal tribal population in southern India.

2014

Pediatric Blood & Cancer

Nimgaonkar, Vivek and Krishnamurti, Lakshmanan and Prabhakar, Hari and Menon, Nandakumar

BACKGROUND: Healthcare delivery for sickle cell disease (SCD) can be challenging, in low resource settings. We studied the feasibility of delivering comprehensive SCD care in a community-based network for remote, economically, and socially disadvantaged tribes in Gudalur, India. PROCEDURE: We reviewed medical records for all patients followed at the Gudalur Adivasi Hospital. We used published quality of care indicators to benchmark screening and routine healthcare maintenance. RESULTS: We screened 9,646 individuals (60.4%) under the age of 30 of a population of 25,000 individuals. Of 111 active patients with SCD, 71% have had at least one annual comprehensive clinic visit at a median visit interval of 57 days. We provided pneumococcal

immunization and penicillin prophylaxis to 56 (50%) patients and HU to 68 (61%). Median spleen size was 1 cm (range 1-6 cm), mean was Hb 9.3 g/dl and we reported a mean of 0.7 painful episodes/year. Premature deaths occurred in 19 patients at a median age of 23 years due to acute chest syndrome, sepsis, severe anemia, stroke, mesenteric infarction, puerperal sepsis, or sudden unexplained death. Healthcare maintenance met 11 of 17 published SCD quality of care indicators. Average cost was 1,343 Indian Rupees (INR) (approximately US$ 25) per hospitalization and 173 INR (approximately US$ 4) per clinic visit. CONCLUSION: High quality comprehensive care for SCD can be delivered for a low income, aboriginal population in India through a community driven network of care. This model can serve as a template for healthcare delivery for SCD in low-income communities. Pediatr Blood Cancer 2014;61:702-705. Â© 2013 Wiley Periodicals, Inc.

122. The fc receptor polymorphisms and expression of neutrophil activation markers in patients with sickle cell disease from Western India.

2013

BioMed Research International

Kangne, Harshada K and Jijina, Farah F and Italia, Yazdi M and Jain, Dipti L and Nadkarni, Anita H and Gupta, Maya and Pradhan, Vandana and Mukesh, Rati D and Ghosh, Kanjaksha K and Colah, Roshan B

Objective. Sickle cell disease has variable clinical manifestations. Activation of neutrophils plays an important role in the initiation and propagation of vaso occlusive crises which can be analysed by determining the expression of neutrophil antigens such as CD16, CD32, and CD62L. The common FcyR polymorphisms (FcyRIIA and FcyRIIIB) are considered to influence clinical presentation. This study focuses on distribution of FcyR polymorphisms and their association with neutrophil activity among the patients from western India. Methods. In this paper 127 sickle cell anemia patients and 58 patients with sickle-Î²-thalassemia (median age 12 Â± 8.58 years) with variable clinical phenotypes along with 175 normals were investigated. FcyRs polymorphisms were analysed by RFLP and AS-PCR. Activation of neutrophils was measured by flow cytometry. Results. The genotypic frequency of the H/R genotype of FcyRIIA and the NA1/NA1 genotype of FcyRIIIB was significantly decreased in patients compared to normals (P-0.0074, P-0.0471, resp.). We found a significant difference in the expression of CD32 and CD62L among the patients as against normals. A significantly higher expression of CD32 was seen in the milder patients with the H/H genotype (P-0.0231), whereas the expression of CD16 was higher in severe patients with the NA2/NA2 genotype (P-0.0312). Conclusion. The two FcyR polymorphisms had significant association with variable phenotypes of sickle cell disease. The expression of CD62L decreased in our patients indicating activation of neutrophils.

123. Influence of single nucleotide polymorphisms in the BCL11A and HBS1L-MYB gene on the HbF levels and clinical severity of sickle cell anaemia patients.

2016

Annals of Hematology

Upadhye, Dipti and Jain, Dipty and Trivedi, Yogesh and Nadkarni, Anita and Ghosh, Kanjaksha and Colah, Roshan

The article discusses a study on the effect of the single nucleotide polymorphisms (SNPs) on the Foetal haemoglobin (HbF) levels and on disease in Indian patients. The study analyses three SNPs in the intronic region of the BCL11A gene and 5 SNPs in the HBS1L-MYB gene in 46 paediatric sickle cell anaemia (SCA) patients (age >4 years) identified by neonatal screening in relation to the HbF levels and disease severity.

124. NOS3 27-bp and IL4 70-bp VNTR Polymorphisms Do Not Contribute to the Risk of Sickle Cell Crisis.

2016

Turkish Journal of Hematology

Verma, Henu and Mishra, Hrishikesh and Khodiar, P K and Patra, P K and Bhaskar, L V K S

The article presents a study which examined the role of NOS3 27-bp variable number tandem repeat (VNTR) and IL4 intron-3 VNTR functional polymorphisms in the development of vasoocclusive crisis (VOC) in sickle cell disease (SCD) in India. Based on the results, NOS3 27-bp VNTR polymorphism is not linked to the risk of frequent crises. The study was approved by the Sickle Cell Institute Chhattisgarh's Institutional Ethics Committee in Raipur, India.

125. Genetics of fetal hemoglobin in tribal Indian patients with sickle cell anemia.

2015

Translational Research: The Journal of Laboratory & Clinical Medicine

Bhanushali, Aparna A and Patra, Pradip K and Pradhan, Smarnika and Khanka, Suraj S and Singh, Sujata and Das, Bibhu R

India tops the list of countries with sickle cell disease (SCD) with an estimated 44,000 live births in 2010 and a prevalence of 10%-33%. In the present study, the first from India, we have investigated the effect of genetic variants in the BCL11A, the HMIP (HBS1L-MYB intergenic polymorphism) locus, in addition to the HBB locus, which are known to be associated with fetal hemoglobin (HbF) levels, a major modulator of the disease phenotype. The present study was conducted on 240 individuals with SCD and 60 with sickle cell trait. Genotyping was performed for the BCL11A rs11886868 and rs34211119; HMIP rs9399137, rs189600565, rs7776196, rs34778774, and rs53293029; HBG2 Xmn1 polymorphism rs7482144; and -68C > T HBD promoter polymorphism. All the 3 quantitative trait loci were associated with HbF levels in Indian patients with SCD. The highest difference was seen in the Xmn1 single-nucleotide polymorphism, which accounted for 11% of the trait variance, the BCL11A rs11886868 for 3.65%, whereas the HMIP rs9399137 for 3.8%. The present study indicates the BCL11A, HMIP, and [beta]-globin region to be associated with increased HbF levels in Indian patient. Further interrogation of these genotypes with respect to pain crisis is warranted in this population, which may help in prognostication, as also a genome-wide association study, which may help uncover new loci controlling HbF levels.

126. Dental considerations in the management of children suffering from sickle cell disease: A case report

2007

Journal of Indian Society of Pedodontics and Preventive Dentistry

Ramakrishna, Y

Sickle cell disease (SCD) is a genetically derived disorder characterized by the presence of an abnormal hemoglobin molecule, designated as hemoglobin S (HbS). It is one of the most common genetic disorder worldwide, with an estimated 70 million people carrying the sickle gene. This article describes the dental considerations in managing a 6-year-old child suffering from SCD (SS type).

127.Benign sickle cell anaemia (a case report).

1984

Journal of postgraduate medicine

Teckchandani, S D and Pandya, P M and Chandes, F P

128.Role of peripheral smear in diagnosing difficult clinical situations in pediatrics

2003

Indian Journal of Practical Pediatrics

Rajajee, S

129.A method for permanent preparation of sickled cells.

1963

Bulletin of the Calcutta School of Tropical Medicine

Ghose, S

130.Homozygous sickle-cell disease in a Punjabi Moslem boy.

1976

British medical journal

Dash, S and Mehta, S and Bhagwat, A G

131.Sickle-cell anaemia in an Indian family in Johore.

1965

The Medical journal of Malaya

Kim, C K and Durham, N A

132.Increased homocysteine level in Indian sickle cell anemia patients

2012

Indian Journal of Clinical Biochemistry

Pandey, S and Pandey, H R and Mishra, R M and Pandey, S and Saxena, R

133. Higher fetal hemoglobin concentration in patients with sickle cell disease in eastern India reduces frequency of painful crisis

2009

European Journal of Haematology

Mashon, R S and Dash, P M and Khalkho, J and Dash, L and Mohanty, P K and Patel, S and Mohanty, R C and Das, B S and Das, U K and Das, P K and Patel, D K

134. Hemoglobinopathies and other congenital hemolytic anemia

2004

Indian Journal of Medical Sciences

Shah, A

135. Presence of atypical beta globin (HBB) gene cluster haplotypes in sickle cell anemia patients of India

2017

Revista Brasileira de Hematologia e Hemoterapia

Nongbri, S R L and Verma, H K and Lakkakula, B.V.K.S. and Patra, P K

136. Compound Heterozygous Hemoglobin D-Punjab/Hemoglobin D-Iran: A Novel Hemoglobinopathy

2014

Indian Journal of Hematology and Blood Transfusion

Gupta, Aastha and Saraf, Amrita and Dass, Jasmita and Mehta, Meenal and Radhakrishnan, Nita and Saxena, Renu and Bhargava, Manorama

Cation exchange high performance liquid chromatography (CE- HPLC) is an excellent tool for the diagnosis of various hemoglobin (Hb) disorders. HbD-Punjab is an uncommon structural Hb variant seen in North-India. Rarely, a compound heterozygous state for HbD-Punjab with high HbA2 has been described. We describe an index case whose CE-HPLC showed a compound heterozygous state for Hb-Punjab/HbD-Iran which was confirmed by family study, acid and alkaline electrophoresis and beta gene sequencing. This case highlights the role of alkaline and acid electrophoresis to resolve common peaks that elute with HbA2 on CE-HPLC. To the best of our knowledge, this compound heterozygous state of HbD-Punjab with HbD-Iran has not been reported earlier.

137. Sickle Cell Crisis Leading to Extensive Necrosis in a Low-Grade Glioma and Masquerading High-Grade Lesion

2008

Pediatric Neurosurgery

Agrawal, Amit and Balpande, D N and Khan, A and Vagh, S J and Shukla, Samarth and Chopra, Sumit

A 9-year-old female child presented with rapid neurological deterioration. Clinical features and imaging findings were suggestive of high-grade malignancy, and hematological investigations were suggestive of sickle cell trait. Histopathology showed features of low-grade malignancy and extensive intratumoral sickling. We hypothesize that the vicious cycle of hypoxia, sickling, thrombosis, ischemia and infarction resulted in the extensive tumor necrosis in the present case causing the initial symptoms and rapid deterioration in the condition of the patient.

138. Obsessive-compulsive disorder associated with sickle beta-thalassemia: A genetic link?

2012

Psychiatry and Clinical Neurosciences

Saraf, Gayatri and Viswanath, Biju and Narayanaswamy, Janardhanan C and Math, Suresh Bada and Reddy, Y C Janardhan

Obsessive-compulsive disorder (OCD) is a common mental illness with 2-3% lifetime prevalence. OCD has a strong genetic basis, but specific genes have not been identified. beta-Thalassemia and sickle cell anemia (SCA) are rare monogenic hereditary disorders caused by mutations in the beta-globin gene located on 11p15.5. An 18-year-old south Indian man presented with 4-year illness characterized by obsessions of symmetry, need for perfection with repeating, ordering, blinking and staring compulsions. To the best of our knowledge, this is the first report of OCD comorbid with SBT. In addition, there was a family history of OCD and TD in this particular case. In a recent study that examined psychiatric comorbidity in a group of children with beta-thalassemia, OCD was found in 15% of the sample. One study in young adults with beta-thalassemia found personality characterized by OC traits, somatization and depression. There are no reports of comorbidity between SCA and OCD. beta-Thalassemia and SCA are caused by specific mutations in the beta-globin gene located at 11p15.5. (PsycINFO Database Record (c) 2016 APA, all rights reserved)

139. Renal papillary necrosis as the first presenting clinical feature in a sickle beta and thalassemic child

2020

Journal of Nepal Paediatric Society

Kumar, J and Chowdary, S and Manjunath, V G and Das, S K and Vuyyuru, M

In sickle cell disease (SCD), the clinical manifestations are due to episodes of vascular occlusion and haemolysis. Most of the children experience vaso-occlusive pain episodes by the age of six years. Renal injury in sickle cell disease referred to as sickle cell nephropathy is a frequent yet under-recognised complication. Renal papillary necrosis (RPN) as the first presentation in SCD is rare. We are reporting a 12 year old child with no prior vaso-occlusive episodes, presenting with renal papillary necrosis due to Sickle Beta and Thalassemia.

140. Arthritis in two brothers: A diagnostic challenge

2018

Journal, Indian Academy of Clinical Medicine

Paul, R and Gayen, B and Mandal, P K and Seth, B C and Sarkar, S and Bandyopadhyay, D and Jana, S and Alamgir, S K

Arthritis or arthralgia may be caused by a variety of rheumatological and non-rheumatological disorders. Systemic disorders presenting only with joint symptoms may cause diagnostic confusion. We here present the case of a 24-year-old male from Eastern India who had prolonged history of joint pain and low back pain. He had visited numerous health facilities in the past and received varying treatment. He was finally diagnosed as sickle-beta disease with multiple bone infarcts. Genetic study revealed the classical HBB: c.20A>T mutation. The

patientâ€™s brother was also found to have homozygous sickle cell disease, albeit with fewer symptoms. Musculoskeletal manifestations of sickle cell disease have been discussed at length.

141. Diagnosis and treatment of cord compression secondary to extramedullary hematopoiesis in patients with beta-thalassemia intermedia

2008

Journal of Clinical and Diagnostic Research

Rahim, F and Keikhaei, B and Zandian, K and Soltani, A

Background: Thalassemia is an inherited autosomal recessive hematological disorder due to genetic defect in synthesis of one of the globin chains. This results in reduced rate of hemoglobin formation and presents as anemia. Depending on whether alpha or beta globin chain is affected they are classified respectively as a thalassemia and Î² thalassemia. If only one Î² globin allele bears a mutation, the disease is called Î² thalassemia minor and if both alleles have thalassemia mutations, the disease is called Î² thalassemia major. Thalassemia intermedia(TI) is a condition intermediate between the major and minor forms. Patients with TI do not receive regular blood transfusions unlike thalassemia major patients. Extramedullary hematopoiesis (EMH) is a compensatory mechanism that occurs in patients with hematological dysfunctions such as Thalassemia Major or Thalassemia Intermedia and Sickle Cell Anemia as a result of continuous erythropoietic stress. Materials and Methods: We report two cases of TI with EMH. One is a 17 year old girl who presented with back pain and leg weakness and a 25 year old man who was referred to the hospital with back pain, paresthesia, urine frequency and impairment of gait. Results: Both the patients were successfully treated with low dose radiotherapy and Hydroxyurea (HU). At the end of the therapy, both the patients had recovered well and were ambulatory. Discussion: Surgical decompression has been the method of choice for the management of the disease. The disadvantages of surgical intervention include risk of excessive bleeding due to high vascularity of the mass. Low dose radiotherapy and hydroxyurea offer better outcomes with reduced morbidity and mortality.

142. Early diagnosis of co-existent ?-thalassemia and alkaptonuria

2013

Indian Journal of Human Genetics

Lodh, Moushumi and Kerketta, Joshi

Since the aggregate incidence of inborn errors of metabolism is relatively high, a high degree of suspicion is essential to correctly diagnose an inborn error of amino acid metabolism. We report a case of alkaptonuria an autosomal recessive disorder that occurs due to deficiency of homogentisic acid oxidasein a Î²-thalassemia infant presenting with reddish discoloration of nappies and clothes, breath holding spells, and microcytic hypochromic anemia. Born to consanguineous cousins, to our knowledge, the combination of Î²-thalassemia and alkaptonuria, which we have described in this baby, has not been reported earlier.

143. Sickle Cell Anaemia Presenting as Acute Renal Failure and Acute Axonal Neuropathy

2013

Thalassemia Reports

Murthy, M and Lakshmi, D and Kavitha, S and Thivya, R

Introduction: Sickle cell disease is an inherited chronic haemolytic anaemia whose clinical manifestations arise from the tendency of the haemoglobin to polymerize and deform red blood cells into the characteristic sickle shape. In our country it is more common in tribals of Central India. Sickle cell anaemia in homozygous state (HbS

is more than 70%) usually present in early childhood. Aim: To evaluate a case of 42-year old male presented with complaints of diarrhea for past 2 days and sudden onset of weakness in both lower limbs and reduced urine output for past one day. He was apparently normal before. Materials and Methods: After the clinical examination, routine blood investigations including complete Hemogram and peripheral smear were done in addition to electrophoresis. Ultrasonogram, MRI Spine and Nerve conduction study were carried out in view of his weakness of lower limbs. Results: On examination the patient was anaemic, Icteric and dehydrated. Hepatomegaly was mild. Tone and power were reduced in lower limbs, deep tendon reflex and plantar reflex were absent in both lower limbs. Ultrasonogram showed hepatomegaly with medical renal disease. MRI Spine was normal. Nerve conduction study done showed severe Axonopathy affecting motor nerves with demyelination. Biochemical investigaions including blood urea, serum creatinine, serum bilirubin, serum LDH were elevated. Complete hemogram showed presence of anaemia, neutrophilic leucocytosis with increased reticulocyte count Peripheral smear picture clinched the diagnosis as sickle cell anaemia with leukemoid reaction. Electrophoresis confirmed the diagnosis with HbS (79.7%), HbA (2.1%), HbF (14.2%), HbA2 (4%). Conclusions: Sickle cell anaemia in hemolytic crisis with acute renal failure and acute axonal neuropathy.

144. Paraplegia due to extramedullary hematopoiesis in thalassemia treated successfully with radiation therapy.

2007

Haematologica

Malik, M and Pillai, L S and Gogia, N and Puri, T and Mahapatra, M and Sharma, D N and Kumar, R

Spinal cord compression due to extramedullary hematopoiesis (EMH) is a rare complication of thalassemia and generally presents as paraparesis with sensory impairment. Complete paraplegia is extremely rare in EMH due to thalassemia although it is known to occur in polycythemia vera and sickle cell anemia. Treatment options mostly include surgery and/or radiotherapy. Whereas cases presenting with paraparesis have been treated with either surgery or radiotherapy with equal frequency and efficacy, almost all reported cases with paraplegia have been treated with surgery with or without radiation therapy. We hereby report a case of thalassemia intermedia with paraplegia treated successfully with radiotherapy.

145. Sickle beta-thalassemia presenting as orbital compression syndrome

2004

Annals of Hematology

Dixit, A and Chatterjee, T C and Papneja, M and Mishra, P and Mahapatra, M and Pati, H P and Saxena, R and Choudhry, V P

Orbital compression syndrome is caused by disorders of varying etiologies involving the orbit and presents with ocular and extraocular dysfunction. Ocular involvement of sickle cell disease is uncommon. A 17-year-old male presented with low backache and proptosis of both eyes of 5 days duration without past history of pain crisis or transfusion. Examination revealed pallor, icterus, bilateral proptosis, conjuctival chemosis, and symmetrical restriction of ocular movements with preserved visual acuity. He was drowsy with no other focal deficits. The fundus showed macular edema, venous engorgement, and no hemorrhage. His peripheral smear showed presence of sickle cells. Computed tomography (CT) scan of the orbit revealed orbital subperiosteal hematomas. CT head images showed epidural hematoma in the frontal lobe. High-performance liquid chromatography (HPLC) and mutation studies revealed sickle betathalassemia in the patient. He was managed with supportive care, transfusions to keep hemoglobin above 10 g/dl, and hydroxyurea. The patient recovered fully and remained well during follow-up of 12 months. Our case was unique for presenting as orbital compression syndrome without any history of vaso-occlusive crisis. Â© Springer-Verlag 2004.

146.First case report of the association of HbE trait and cold agglutinin disease

2011

Internet Journal of Hematology

Chandrashekar, V and Soni, M

This is the first report of the association of cold agglutinin disease with HbE trait. The patient was 58 year old male from Assam, India. Thalassemia, sickle cell disease and sickle-HbC have been found to be associated with cold agglutinin disease. Cold agglutinin disease has also been detected in patients with polycythemia vera. Erythrocytes in these disorders are likely to be immature and express more big "I" and little "I" antigens, the target antigens for cold agglutinins. Increased expression of big "I" and little "i" has been demonstrated in sickle cells. Conceivably, the increased expression of "I" and "I" in sickle cell disorders, thalassemia and HbE and polycythemia vera might render the erythrocytes in these disorders more vulnerable to cold agglutinins and hemolysis.

147.High HB F level in sickle beta thalassemia patient leads to milder sickle phenotype

2020

Indian Journal of Hematology and Blood Transfusion

Gamit, M J and Patil, R and Rahim, S and Krishna, R

Aims & Objectives: High HB F level in sickle beta thalassemia patient leads to milder sickle phenotype. Patients/Materials & Methods: HbS-Î² thalassemia is a sickling disorder of varying severity, which results from compound heterozygosity for sickle cell trait and Î² thalassemia trait. clinical features and hematologic findings are highly variable depending on the severity of Î² thalassemia.Herein, we report a case of HbS-Î² thalassemia with High Hb F level. A 12 year old boy has been followed up in our hospital for last 2 years. He is a known case of HbS-Î² thalassemia. Hematological parameters like CBC,Reticulocyte count and Peripheral blood smear was performed.Biochemical parameters like RFT,LFT and LDH was performed. He had recurrent admissions previously with complains of joint pains, fever accompanied by abdominal pain.6 months ago, he was started on hydroxyurea 500 mg and this led to complete resolution of his symptoms. We also checked his Hb electrophoresis. Results: His hemogram showed Hb 8.6 gm/dl,Mcv 67.6 fl,MCH 22.5 pg, MCHC 33.2 gm/dl, TLC 9.3 Ã— 103,Platelet count 139 Ã— 103. On peripheral smear, RBC picture showed Microcytes, target cells and few sickle cells.Reticulocyte was 5.24%.Biochemical assessment showed Creatinine 0.4 mg/dl, LDH 720 U/L,Total bilirubin 4.3 mg/dl,Direct bilirubin 0.5 mg/dl and indirect 3.8 mg/ dl.Hb electrophoresis showed Hb F- 33.3%,Hb A2-3.9%, Hb S - 50.4%. Discussion & Conclusion: Discussion: Haemoglobinopathies occurs due to structural defect in the globin gene. Thalassemias are due to defect in the production of globin chain. The Hb S is of clinical importance because of their worldwide prevalence. This is the most common form of sickle cell disease in people of Mediterranean descents.In India it is most prevelent in North-East. A case of Compound heterozygous for Hb S- Î² thalassaemia was previously reported with severe anaemia, massive hepato-splenomegaly and acute Chest syndrome. But in our case patient showed large Hb F response to hydroxyurea and there was significant improvement in his clinical symptoms. Conclusion: This patient shows large Hb F response to hydoxyurea. we postulate that this led to significant improvement in his clinical symptoms. We also wanted to discuss the morphology picture and Hb electrophoresis for academic purposes.

148.Osteomyelitis and pyomyositis due to pseudomonas aeruginosa in a child with sickle Î²0-thalassemia

2011

Journal of Pediatric Hematology/Oncology

Krishnamurthy, S and Thimmaiah, S and Ramesh, A and Biswal, N and Menon, J and Elangovan, S

Sickle cell osteomyelitis is usually due to Salmonella or Staphylococcal etiology. Pseudomonas as a cause of sickle cell osteomyelitis is rare. Similarly, pyomyositis is a rare complication in children with sickle cell disease and few cases have been reported, predominantly due to Staphylococcus. We describe an 8-year-old boy who presented with high-grade fever and tender, swollen left thigh. There was a history of intramuscular injections in the left thigh. He also had severe anemia, hepatosplenomegaly, and laboratory evidence of hemolysis. Hemoglobin electrophoresis showed sickle Î²-thalassemia. Magnetic resonance imaging of the left thigh showed evidence of osteomyelitis with pyomyositis. Surgical drainage of the pus was done and Pseudomonas aeruginosa was isolated. He was treated with intravenous antibiotics for 8 weeks. The child had a protracted course of illness with development of pathologic fracture of the femur. Clinicians need to be aware of Pseudomonas infection as a complication in children with sickle cell disease, as this affects therapeutic decisions, including the choice of antibiotics. Copyright Â© 2011 by Lippincott Williams & Wilkins.

149.Idiopathic facial swelling secondary to sickle cell anaemia

2012

BMJ Case Reports

Moghe, S and Pillai, A and Guru, K N and Nair, P P

Sickle cell disease is a common inherited autosomal disease that is characterised by abnormally shaped (sickle-shaped) red blood cells (RBCs). It can involve virtually any organ system. The clinical manifestations of sickle cell disease vary and are classified as vaso-occlusion, chronic anaemia and infection. The imaging appearances of central nervous system and musculoskeletal involvement by sickle cell disease have been well documented; however, involvement of the head and neck region is often unreported, although it is not uncommon. In the head and neck, sickle cell disease can involve the inner ears, orbits, paranasal sinuses, bones, lymph nodes and vessels. This paper describes a case of idiopathic facial swelling associated with sickle cell disease in a young patient. Copyright 2012 BMJ Publishing Group. All rights reserved.

150.Sickle cell hepatopathy

2008

Indian Journal of Pathology and Microbiology

Bandyopadhyay, R and Bandyopadhyay, S and Dutta, A

Sickle cell hepatopathy is a well-documented entity that ranges from the self-limiting hepatic right upper quadrant syndrome to the potentially lethal intrahepatic cholestasis and acute hepatic sequestration syndromes. We describe a 26-year-male with homozygous sickle cell disease who had this unique hepatic presentation and was documented to have characteristic findings of cholestasis, portal inflammation and sinusoidal dilatation on histopathology.

151.Sickle cell hepatopathy

2011

Indian Journal of Gastroenterology

Kothari, R and Shetty, S

Sickle cell hepathopathy encompasses a range of hepatic pathology arising from a wide variety of insults to the liver in patients with sickle cell disease. It occurs predominantly in patients with homozygous sickle cell anemia, and to lesser extent in patients with sickle cell trait, Hb SC disease and Hb S Î² thalassemia. It is a well-documented entity that ranges from the self-limiting hepatic right upper quadrant syndrome to the potentially lethal intrahepatic cholestasis and acute hepatic sequestration syndromes. Chronic liver disease in SCD may be due to hemosiderosis and hepatitis. It is possible that repeated small, clinically silent microvascular occlusions occur throughout the life

of a SCD patient, eventually leading to liver fibrosis, superimposed on other causes of chronic liver disease. We describe a 38-year-male with homozygous sickle cell disease who had this unique hepatic presentation and was documented to have characteristic findings of portal inflammation and sinusoidal dilatation on histopathology.

152. Sickle cell crisis mimicking tumour lysis syndrome

2016

Indian Journal of Hematology and Blood Transfusion

Khaddar, S and Chhabra, P

Introduction and Background: Homozygous sickle cell anemia usually presents as sickle cell crisis at young age, usually around 2-10 years and very rarely in adulthood. Sickle cell trait is largely asymptomatic, rarely painless hematuria may be the only symptom. We present a case of a 19 year old boy who presented for the first time with sickle crisis with his clinical profile mimicking tumor lysis syndrome. Patient/Material and Methods: A 19 year boy presented with fever and generalized body pain for 15 days, yellowish discoloration of eyes and urine for 5 days, decreased urine output for 3 days and breathlessness and altered sensorium for last 2 days. There was no history of bleeding, previous similar episodes or familial predisposition. There was no lymphadenopathy, liver and spleen were mildly enlarged. His Hb was 4.3 g/dl, TLC-1.38 lacs/mm3 with many precursors along with deranged LFT, RFT, hyperkalemia, hyperuricemia and hypocalcaemia with negative paracheck, leptocheck and viral screen. Results: The initial clinical picture was suggestive of acute leukaemia with tumour lysis syndrome. However, his GBP and bone marrow analysis, done few days after stabilization, revealed multiple sickle shaped cells with nucleated RBCs, high reticulocyte count and hypercellular marrow with erythroid hyperplasia respectively. Thus, a HPLC was performed which showed sickle cell trait pattern. Meanwhile patient was managed with haemodialysis, blood support and other conservative measures. Conclusions: Sickle cell syndromes are remarkable for their clinical heterogeneity. Some patients remain virtually asymptomatic into or even through adult life, while others suffer repeated crises requiring hospitalization from early childhood. Sickle cell trait is virtually asymptomatic that is why adult age, very high leukocyte counts with lab parameters of tumour lysis were misleading points in our case. However, GBP and Bone marrow aspiration after patient stabilization helped to reach correct diagnosis.

153. Pregnancy in a sickle cell disease patient: A nightmare!

2020

Journal of SAFOG

Doshi, B and Mehendale, M A and Nayak, A H and Bhosale, A A and Mulik, S

Aim: To discuss the effect of pregnancy in sickle cell disease (SCD) patients and its associated complications. Background: Sickle cell disease is the most common inherited disorder worldwide and in certain regions of India with varying clinical severity and potentially serious complications. Sickle cell disease can magnify complications during pregnancy and in turn negatively influence the pregnancy outcomes. The physiological adaptations during pregnancy that occur in the circulatory, hematologic, renal, and pulmonary systems can overburden organs that already have chronic injuries secondary to SCD, thus increasing the rate of obstetric complications like miscarriage, anemia, preeclampsia, worsening of vaso-occlusive crisis, and acute chest syndromes. Case description: A 23-year-old Indian primigravida patient, known case of SCD with anemia and splenic infarct with h/o multiple blood transfusions. The patient presented at 12 weeks with intrauterine fetal demise and was medically aborted. The post-abortion patient was posted for splenectomy as she had episodes of hemolytic jaundice. Post-splenectomy patient further developed bowel obstruction and thrombus formation in the infrarenal part of inferior vena cava (IVC). She was again operated and for obstruction and the band was removed. For thrombi, patient was given low molecular weight heparin (LMWH). The patient was finally discharged on tb. hydroxyurea and other antibiotics. Conclusion: The higher rate of complications occurs in women with sickle cell crisis exaggerated by underlying factors such as long-term anemia and pregnancy increases the risk further. Thus,

a multidisciplinary approach with regular follow-up of SCD patients since the time of preconceptional time is important to avoid pregnancy-related complications and also for a better pregnancy outcome. Clinical significance: The physiological changes of pregnancy like increased blood volume, increased metabolic demand, increased blood viscosity, and hypercoagulability get aggravated in SCD patients leading to increased incidence of complications. Prepregnancy anemia and other complications of a mother can further affect the outcome, thus preconceptional counseling is a crucial part of management.

154.Haemoglobin SD disease - Rare case of jaundice

2012

Journal of the Indian Medical Association

Ghosh Prof., U C and Sen Prof., K and Narayan, A and Banik, K K and Saha Prof., P K

A 15 years old Muslim female presented with moderate anaemia, mild jaundice and hepatosplenomegaly with no history of blood transfusion in the past. Routine examination was suggestive of haemolytic jaundice. High pressure liquid chromatography (HPLC) electrophoresis of the patient's blood showed haemoglobin (Hb) SD disease. As it is a double heterozygous disease, family screening was done. It showed that the father was sickle cell trait. Mother was Hb D trait. Both the brothers were sickle cell trait and the only sister was normal. Hb SD disease is a very rare variety of haemoglobinopathy and the case is presented here due to its rarity.

155.Portal hypertension associated with sickle cell disease

2007

Indian Journal of Gastroenterology

Kumar, S and Joshi, R and Jain, A P

We report a 12-year-old girl with sickle cell disease who presented with pain in abdomen, fever, joint pain and hematemesis. On examination she had mild jaundice and splenomegaly. Upper GI endoscopy showed esophageal varices. She was treated with variceal band ligation, and is well on folic acid supplements and propranolol.

156.Variable phenotype+- of Hb SD-Punjab disease in two siblings

2019

Pediatric Hematology Oncology Journal

Aggarwal, P and Mishra, O P and Gupta, V

ABSTRACT Background: Sickle cell Disease (SCD) is the most common inherited condition globally. SCD includes both the homozygous i.e. HbSS as well as the heterozygous forms i.e. HbS in combination withÎ² thalassemia (Hb SÎ²),Hb C (Hb SC), Hb O Arab(Hb SO Arab), Hb E (Hb SE) and Hb D-Punjab (Hb SD-Punjab).The clinical presentation HbSD disease is as severe as homozygous Hb SS but few cases with mild presentation have been reported. Individuals with high fetal haemoglobin (HbF) tend to have a mild presentation as compared to those with low levels of the same. Case: A 3 year female, resident of Madhya Pradesh born of a non consanguinous marriage, presented with complaints of progressive paleness for 2 years, requiring multiple units of blood transfusion. She had history of blood transfusion 17-18 times in last 2 years. On examination, the child had pallor with hepatospenomegaly. Thus, a provisional diagnosis of Chronic Hemolytic anemia possibly Thalessemia major was kept. At the time of presentation to our outpatient her haemoglobin was 12.2 with MCV 94.7 and RDW 18% (history of blood transfusion 4 days back), there was indirect hyperbilirubinemia (total bilirubin 1.8/ indirect bilirubin 1.3) and corrected Reticulocyte count was 1.8%. As her sickling test was positive we did High pressure liquid chromatography (HPLC) after 1.5 months of blood transfusion, which was suggestive of compound heterozygous Hb SD disease (HbF 16.1%, HbA2 0.7%, Hb A 41.8%, HbS 11.7% and HbD 23%).

Whenher elder brother (5-year, male) was screened, his HPLC was also suggestive of a compound heterozygous Hb SD disease (HbF 30.4%, HbA2 0.5%, HbA 2.9%, HbS 19.3, and HbD 43.5%)although he was asymptomatic with no history of blood transfusion and no hepatosplenomegaly. HPLC of father was suggestive of Heterozygous Sickle cell disease (HbF 0.5%, HbA2 2.3%, HbA 52% and HbS 39.6%) and of mother was suggestive of Heterozygous HbD status (HbF 0.8%, HbA2 0.6%, HbA 52.2%, HbD 36%). Mutational analysis of brother confirmed the diagnosis of compound heterozygousHb SD-Punjab disease. Conclusion: Various factors affect the clinical phenotype of sickle cell disease. Although our patient had a severe transfusion dependent phenotype her brother was asymptomatic as his HbF levels were high. The cause of high HbF levels in the elder brother could not be ascertained. Thus, we conclude that even two siblings can have a variable clinical severity with respect to HbF levels. Genetic counselling is of utmost importance to prevent a severe transfusion dependent sickle cell disease.

157.Persistent splenomegaly in sickle cell anemia: An unusual finding

2019

Indian Journal of Hematology and Blood Transfusion

Aggarwal, N and Sahu, P and Kumar, V and Marwah, S

Aims & Objectives: To study persistent splenomegaly in sickle cell anemia. Patients/Materials & Methods: A 23 year old female presented with complaints of fever, breathing difficulties and pain in upper limbs and back since 2 days. She had past history of similar complaints on and off. On examination, she had pallor, icterus and splenomegaly. Detailed haematological work up including HPLC was done. It's correlation with clinical details will be presented. Results: She was found to be HbS on hematological workup. Discussion & Conclusion: Sickle cell anemia is caused by a globin chain defect leading to hemolyticanemia and recurrent sickling crisis due to increased sludging and thrombosis in small vessels. Patients develop splenic infarcts, which over time cause autoplenectomy. Most patients have autosplenectomy by the age of 8 years. Persistent splenomegaly is found in about 10% patients after the age of 10 years which may be due to various environmental and genetic factors.

158.Hepatic sickling crisis mimicking recurrent cholangitis

1999

Indian Journal of Gastroenterology

Mehta, S and Nagral, A and Sucheta, V K and Nagral, S and Gopal, S and Joshi, A S and Krishnamurthy, S

A 22-year-old man with homozygous sickle cell disease presented with recurrent fever, right upper quadrant pain and jaundice. Liver biopsy confirmed the diagnosis of hepatic sickling crisis; the symptoms responded to hydroxyurea therapy. Hepatic vasocclusive crisis can diagnosed on liver biopsy, and need not be a diagnosis of exclusion.

159.Haemoglobin penang: A novel, clinically silent but not insignificant beta-globin variant

2018

British Journal of Haematology

Hsu, C.H.-W. and Besser, M and Langdown, J

Haemoglobin abnormalities are the most frequent genetic disease, with inherited haemgolobin disorders affecting up to 7% of the global population. Over 1000 haemoglobin variants have been identified globally, all of which are recorded on the database 'Hbvar' (http://globin.cse.psu.edu/hbvar/menu.html). Although homozygosity of the commonest variant, HbS [b6: Glu>Val], gives rise to the debilitating phenotype of sickle cell disease, at least 50%

of variants are clinically silent. Their detection therefore heavily relies on screen-ing programmes, mainly antenatal screening in the UK but also pre-marital screening in countries like India and Saudi Arabia. We report a novel haemoglobin variant with a beta-chain amino acid substitution at codon 78 [b236, T>C], detected through antenatal screening via high-performance liquid chromatography (HPLC) in an otherwise healthy and asymptomatic 38-year old female of South-East Asian ancestry. The variant, named Hb Penang, under-went further characterization through capillary zone electrophoresis (CZE), Sanger sequencing, stability testing and isoelectric focusing (IEF). We reflect on the increasing detection of clinically silent haemoglobin variants resulting from the NHS Sickle Cell and Thalas-saemia Screening guidelines, and discuss the implications for both the patient, her family and the wider public.

160. An unusual case of bilateral pontine infarct in a patient with dengue fever having multiorgan dysfunction

2020

International Journal of Stroke

Doshi, D and Agarwal, M

Background And Aims: Haemorrhagic strokes are a known thing in Dengue fever due to increased propensity to bleeding in view of reduced platelet counts. However, Dengue fever causing ischaemic stroke is not very common and not well understood. Here we report an interesting case of Dengue Fever presenting with bilateral pontine infarcts with near complete recovery. Methods: We describe a case report of a 15-year-old admitted at a tertiary care hospital in India. Results: Young girl with sickle cell trait, presented with fever for fifteen days prior to admission. On initial examination, she did not have any neurodeficits. She later developed status epilepticus following which she was intubated and ventilated. MRI of the brain showed bilateral pontine infarcts with diffuse leptomeningeal enhancement. Elisa for Dengue IgM was positive with ferritin levels of 21800 mcg/L. She had pancytopenia with mildly deranged liver parameters. APLA was negative. CT Angiogram did not reveal any evidence of vasculitis. Cerebrospinal fluid showed 1 lymphocte with 403mg/dl proteins, with multiplex nucleic acid test negative for Herpes Simplex virus and Varicella Zoster Virus. PCR for Japanese Encephalitis Virus was also negative. Hemophagocytic lymphohistiocytosis genetic testing was negative. Cardiac evaluation was negative for any cardiac source of embolus. She was treated with pulse dose corticosteroids and aspirin 75mg. Post-extubation, she only had left lower motor neuron facial palsy. Conclusions: Ischemic stroke as a complication of dengue infection has rarely been reported. One of the postulated pathogenetic mechanism for ischemic stroke in dengue fever is meningovasculitis. Early initiation of therapy will help to improve the clinical outcome.

161. Retinitis pigmentosa patients with sickle cell disease and dextrocardia and situs inversus syndrome.

2001

Indian journal of ophthalmology

Madhavan, C and Bhende, P and Gopal, L and Vasanthi, S B and Kumaramanickavel, G

Two cases of retinitis pigmentosa (RP) with associated sickle cell disease in one patient, and situs inversus totalis in the other are reported. To our best knowledge, these associations have never been reported in RP.

162. Sickle cell hemoglobin - D Punjab disease (compound heterozygous state)

2000

Indian Journal of Hematology and Blood Transfusion

Tyagi, S and Marwaha, N and Parmar, V and Basu, S

Compound heterozygous state is a very rare condition characterized by coinheritance of two abnormal hemoglobin gene in the same individual resulting into clinically significant disease. We report here a case of sickle cell hemoglobin - D Punjab disease (compound heterozygote). An eight year old female child, resident of Punjab was presented with moderate hemolytic anemia and hepatosplenomegaly. Initially it was considered as a case of sickle cell anemia but subsequently confirmed as Hemoglobin S-D Punjab disease using agar gel electrophoresis.

163. Falciparum Malaria Infection in a Case of Sickle Cell Trait; Unbalancing the Balanced Polymorphism

2013

Indian Journal of Hematology and Blood Transfusion

Amale, Amar and Acharya, Sourya and Shukla, Samarth and Dubey, Sameeksha

Suffers of Sickle cell trait are protected against plasmodium falciparum malaria because of the law of balanced polymorphism. We present a case of sickle cell trait infected with severe falciparum malaria unbalancing of balanced polymorphism

164. Massive ossifying fibroma of the mandible in a child

2013

Journal of Indian Association of Pediatric Surgeons

Bajpai, Minu and Goel, P and Bhutia, O and Gupta, Anand and Seth, A and Gupta, A and Pawar, D

An interesting case of large ossifying fibroma of the mandible in a child with a sickle-cell trait is reported.

165. An autopsy case of sudden death in a patient with sickle cell disease

2007

Indian Journal of Hematology and Blood Transfusion

Devi, M and Subadani Devi, S and Debnath, K and Devi, Th.M. and Singh, H N

An autopsy finding of sudden death due to disseminated intra-vascular sickling of RBCs in a young adult male from Madhya Pradesh while undergoing army recruitment rally, is reported because of its rarity in this part of the country. Â© Indian Society of Haematology & Transfusion Medicine 2007.

166. Serendipity: A rare discovery of Haemoglobin D-Iran in an Indian female during routine antenatal screening for Î²-Thalassemia

2015

Journal of Clinical and Diagnostic Research

Chandel, R S and Roy, A and Abichandani, L G

Haemoglobin D is a rare form of haemoglobinopathy in homozygous form. However, the heterozygous form of the disease is clinically silent and relatively easier to find in North-West India, Pakistan and Iran. Haemoglobin D is sometimes found to be coexistent with Haemoglobin S and/or Thalassaemia leading to clinically significant conditions like sickle cell anaemia with mild to moderate splenomegaly. In India the more prevalent form is Haemoglobin D-Punjab (also known as Hb D- Los Angeles) which has a prevalence of 2% in Punjab and around 1% in Gujarat. However, the variant, Haemoglobin D- Iran is very rare in India in heterozygous as well as homozygous forms. This report is of a 36-year-old female, who visited for an antenatal check up. On analysing

the blood sample using Agarose Gel Electrophoresis in Alkaline media, the migration of abnormal haemoglobin to haemoglobin S/D/G region was observed. Sickle cell solubility test was negative. On capillary electrophoresis, peak in the Haemoglobin D Zone was seen.

167. Phenotypic expression of HbO Indonesia in two Indian families and its interaction with sickle hemoglobin.

2017

Indian Journal of Pathology & Microbiology

Gupta, Amar Das and Nadkarni, Anita and Mehta, Pallavi and Goriwale, Manju and Ramani, Manisha and Chaudhary, Pradnya and Mehrotra, Vishal and Colah, Roshan

Background: Alpha globin chain variants are clinically significant since they directly influence the structure and function of the hemoglobin (Hb) molecules they constitute, either in combination with normal beta globin chains or with variant beta chains, thereby altering the morbidity and mortality associated with the resultant hemoglobinopathies. We describe here two unrelated families from Madhya Pradesh who had a nondeletional alpha-chain variant, HbO Indonesia (CD116 G â†' A). Members of one of the two families also had coinheritance of sickle hemoglobin (HbS).Aims: The aim was to study the phenotype of HbO Indonesia and its interaction with HbS.Materials and Methods: Hb electrophoresis, high-performance liquid chromatography (HPLC), covalent reverse dot blot hybridization, amplification refractory mutation system, multiplex polymerase chain reaction, and direct gene sequencing were used to identify and characterize the variant Hbs.Results: The abnormal Hb moved in HbS region in Hb electrophoresis at alkaline pH but gave an abnormal peak in HPLC with a retention time (RT) of 4.86-4.89 min. In two members of the family with coinheritance of HbS, it produced small additional abnormal Hb peaks (4.6% in heterozygous and 11.9% in homozygous member) in HPLC with a longer RT (5.15-5.17 min) possibly resulting from a combination of HbO Indonesia alpha chain with HbS beta chain.Conclusions: It appears that depending on the zygosity of HbS, HbO Indonesia would subtract a variable amount of HbS beta chain from the total pool, thereby potentially reducing the clinical severity of HbS disease. HbO Indonesia per se does not cause anemia or alter the red cell indices.

168. A rare hemoglobin variant, Hb Belliard.

2017

Baylor University Medical Center Proceedings

Murthy, Stacey and Benavides, Raul

There are many documented variants of hemoglobin; however, other than a limited number (such as sickle cell disease), very few are known to have any clinical significance. As advances in detection and identification continue through gel electrophoresis, capillary electrophoresis, and DNA sequencing, more rare variants are identified. Without case reporting, the significance of these variants will remain unknown or continue to be thought of as insignificant. Here we report a rare hemoglobin variant, Hb Belliard, which was detected in a 68-year-old Indian immigrant to the United States. He presented with elevated hemoglobin and was found to have a unique peak on capillary electrophoresis. The specimen was sent for sequencing and was subsequently found to have Hb Belliard. Currently, Hb Belliard is thought to be insignificant.

169. Hematoidin Pigment with Bone Marrow Necrosis in Sickle Cell Anemia

2020

Indian Journal of Hematology and Blood Transfusion

Aggarwal, C and Dass, J and Saraf, A and Sharma, Ajay and Kotwal, J and Chetan, Aggarwal and Jasmita, Dass and Amrita, Saraf and Sharma, Ajay and Jyoti, Kotwal and Aggarwal, C and Dass, J and Saraf, A and Sharma, Ajay and Kotwal, J

170.Fulminant hepatitis A in children with sickle cell disease.

2002

Indian pediatrics

Renge, R L and Dani, V S and Chitambar, S D and Arankalle, V A

171.Multiple myeloma in a patient with sickle cell anaemia.

1986

The Journal of the Association of Physicians of India

Sarma, P S and Viswanathan, K A and Mukherjee, M M

172.Chronic myelocytic leukaemia in a patient with sickle cell anaemia.

1986

The Journal of the Association of Physicians of India

Sarma, P S and Chawda, B K and Das, S R

PROGRAMS

1. **Gujarat state sickle cell program: A public-private partnership in comprehensive community based care delivery**

   2011

   American Journal of Hematology

   Italia, Y M and Mehta, V I and Raicha, B K and Jah, B M and Mishra, U and Gandhi, S and Dave, P

Background: In India, sickle cell gene is highly prevalent in the indigenous groups such as the scheduled tribes in whom the carrier frequencies range between 5-40%1. The Constitution of India recognizes these communities as being extremely disadvantaged. They account for 84.3 million (8.2%) of India's population of over 1.2 billion individuals. Gujarat state has tribal population of 6.16 million individuals, which represents 14.75%, of the total population of 55 million individuals. Thus, sickle cell disease represents a major public health problem in Gujarat which requires a comprehensive community based approach. Aim: To develop a comprehensive community statewide sickle cell program integrated into the public health and primary care network. Methods: Starting in 1984 Valsad Raktadan Kendra a nonprofit agency undertook extensive community based screening and comprehensive care sickle cell programs in collaboration with the state public health and primary care network. In 2006, the Government of Gujarat, in a public-private initiative, nominated Valsad Raktadan Kendra to implement a Sickle Cell Anemia Control Program initially in the 4 districts of south Gujarat and subsequently in all the 12 districts with a high concentration of Tribal populations. Community based testing and treatment centers were established throughout the region integrated into the public health care infrastructure. Extensive training was carried out for health care providers in screening, counseling and comprehensive care. Multipurpose health workers were trained for counseling, case management and coordination of care. Facilities were also established for prenatal diagnosis and New Born Screening for sickle cell disease. Results: Using the extensive network of state run health centers, we established 414 centers for the diagnosis, treatment and counseling for sickle cell disease and trait. We trained 85 counselors and all multipurpose health workers employed in the state health service to implement routine treatment of sickle cell disease and to provide counseling and coordination virtually at the doorstep of the patient. Prenatal diagnosis is currently available at Valsad, a tribal district head quarter. Currently, we are integrating newborn screening into the state sickle cell program. Of the 1,060,000 screened individuals, 12.76% are sickle cell heterozygote and 0.76% had sickle cell disease. These data suggest that, in the state of Gujarat alone, there are over 50,000 individuals with sickle cell disease and 1500 new births with sickle cell disease every year. Care is provided through the network of primary health care and through private practitioners. Guidelines for clinical care are being implemented. Conclusions: We have demonstrated the feasibility of implementing a comprehensive community based sickle cell program in a developing country for a very large disadvantaged population.

2. **Developing A Thalassemia Day Care Centre In A Government Medical College With Aid From National Health Mission: Outcomes And Challenges**

   2018

   Pediatric Hematology Oncology Journal

   Verma, N and Chandra, T and Kumar, A

Background: Thalassemia is the most common chronic haemolytic anemia in India, with an estimated disease burden of 100,000. Of the 10,000 to 12,000 thalassemic children born annually in India, very few are optimally managed. Due to the high costs and poor local availability of treatment, the WHO estimates that nearly 90% of

transfusion dependent patients are not adequately transfused. Reporting on how the Thalassemia Day Care facilities were developed at a government medical college hospital in Uttar Pradesh and the profile and outcome of children with thalassemias at this new center were the objectives of the study Methods: In October 2016, a Thalassemia Day Care Center was established in the Department of Pediatrics, KGMU, Lucknow with financial aid from National Health Mission (NHM). Children with any form of inherited hemoglobinopathy were registered and provided free of cost transfusions with leucodepleted packed RBC (without any replacement donation) and iron chelation if indicated. Financial support for the services was provided by a recurring grant from NHM. Results: Over the last 22 months, 103 children with various haemolytic anemias from Uttar Pradesh, Bihar and Nepal (Figure 1) have been registered in the Day Care Center (median age 24 months, M:F 2.3:1). The diagnosis distribution of these children is as follows: Thalassemia Major 75, Thalassemia Intermedia 20 (EÎ² Thalassemia 7, SÎ² Thalassemia 5, Others 8), Sickle cell anemia 1, Congenital Dyserythropoetic Anemia 1, Others 6. Ninety two percent children are adherent with their regular transfusions, while 8% (8/103) children abandoned regular transfusions, 7 of whom have died. The commonest reason cited for abandonment and missed appointment days were inability to travel long distances. Iron chelation with oral Deferasirox has been started in 35 children. Conclusions: There is a need to develop Thalassemia Day Care facilities in resource poor, less advanced countries at many new centres so that poor patients need not travel long distances for treatment. Such centres can be established and run successfully with financial support from government bodies like NHM. Figure 1 District-wise distribution of children registered in the Thalassemia day care centre KGMU (Red triangle: Abandoned children, Black triangle: Children in regular follow up)

3. **Burden of thalassemia in India: The road map for control**

   2017

   Pediatric Hematology Oncology Journal

   Colah, R and Italia, K and Gorakshakar, A

The thalassemias and structural haemoglobin variants are the commonest monogenic disorders globally. India has a huge burden with an estimated 100,000 patients with a Î² thalassemia syndrome and around 150,000 patients with sickle cell disease, but few among them are optimally managed, and allogeneic stem cell transplant is unaffordable for the majority of families. A feasible option for control is to promote education and awareness programmes, intensify screening in all the states with micromapping to assess the true burden, and develop adequate facilities for genetic counselling and prenatal diagnosis in public sector Institutions. Government and non-government organizations have been working towards this goal for the last 3 to 4 decades but community control in a vast and diverse country is challenging and a national programme reaching all rural regions where almost 70% of the population resides is yet to begin. Strategies to control thalassemia need to include 1) Educating health professionals, school and college students, pregnant women and the population at large 2) Establishing prenatal diagnosis facilities in different regions of the country 3) Setting up a greater number of Day Care Centres for managing existing thalassemia patients 4) Developing cost-effective facilities for stem cell transplantation across the country. This review explores strategies by which Central and State Governments, NGOs, Parents-Patients Societies and Corporate Houses can work together to successfully reduce the burden of hemoglobinopathies in India. Guidelines for implementation of such a national programme have recently been prepared by the National Health Mission, Ministry of Health and Family Welfare with the help of several experts in the country.

4. **Sickle cell anaemia-community control programme amongst tribal groups from satpuda hilly ranges in maharashtra, India**

   2012

   Indian Journal of Hematology and Blood Transfusion

   Kate, S L and Yeola, G H and Dalvi, P N and Kulkarni, G T and Prabhune, Y S

Abstract: Amongst all the tribal area of Maharashtra Sickle Cell Disorder is very common amongst Bhill and Pawara tribal population groups residing in the Satpuda hilly ranges (trait prevalence 1:5). Considering counselling is the only alternative, to control the disease, we have established a community control centre in high risk area located between 3rd and 4th hilly ranges of Satpuda hills (at Roshmal Budruk, Tal. Dhadgaon, Dist. Nandurbar Maharashtra state. We provided accurate diagnosis, possible treatment, follow-up counselling. We have now 1501 sickle cell patients under our medical supervision. Counselling is provided to patients, parents and public from this area. Details will be described in the presentation.

5. **Gazelle, a promising point-of-care diagnostic for hemoglobin disorders in India: Bridging the gap in control program**

   2019

   American Journal of Tropical Medicine and Hygiene

   Rajasubramaniam, S and Kumar, R and Shrivas, S and Verma, A K and Thota, P and Bharti, P and Rocheleau, A and Witte, T and Uikey, R and Hasan, M N and Gurkan, U A and Das, A

Sickle Cell Disease (SCD) and thalassaemias are the two prevalent genetic disorders causing anaemia and associated complications. The prevalence of both SCD and carriers varies from 5-35% among ethnic groups and Scheduled caste communities in 5 states namely Madhya Pradesh, Gujarat, Maharashtra, Odisha, Chhattisgarh and Andhra Pradesh in India. Mass screening involves solubility test followed by confirmation by high-performance liquid chromatography (HPLC) or haemoglobin electrophoresis. Absence of public health diagnostic facilities results in high morbidity and mortality among undetected patients. Evaluatory phase I studies on â€œGazelleâ„¢ â€, a microchip-based cellulose acetate electrophoresis device were conducted in tribal-dominated Madhya Pradesh and Chhattisgarh states of. Gazelleâ„¢ is a rapid (<10 minutes) and easy-to-use test that can be carried out using a finger-prick volume of blood. Blood samples were collected from 300 patients enrolled in a pilot study at a high prevalence setting (ICMR-NIRTH, India). Each sample was tested with Gazelleâ„¢, and the results were compared to electrophoresis and HPLC. A total of 295 patient samples were included in the analysis (3 samples were excluded due to incomplete runs; sequencing results are pending for 2 samples). Phase II testing with improved Gazelleâ„¢ is ongoing and results will be presented at the Conference. Of the 295 tested samples, 4% were HbSS and HbSÎ²-thal, 21% were sickle cell trait and 74.9% were of normal (HbAA) category. Gazelleâ„¢ showed high accuracy (100%), sensitivity and specificity in detecting SCD (HbSS) and Î²-Thalassemia, sickle cell trait (HbAS) when compared with standard screening tests. Microchip electrophoresis technology is a promising, low-cost ($2 per test), rapid, and accurate method for detecting hemoglobin disorders such as SCD in limited resource settings in India. Gazelle aims to bridge the gap in diagnosis of sickle cell and hemoglobin disorders in healthcare.

6. **Sickle cell screening programme in Chhattisgarh, India**

   2012

   American Journal of Hematology

   Patra, P K

A programme designed to detect the sickle cell trait and sickle cell diseases has been screened 736,000 in Raipur, Mahasamund, Durg district, Chhattisgarh State, India between October 2007 and October 2011. The methods which have involved sampling all children aged 3-15 years of the villages in Raipur, Mahasamund, Durg district, Chhattisgarh State, involved initial screening by solubility tests on fingerprick samples in the villages followed by vane puncture on all subjects with positive solubility tests. These samples were transferred to the laboratories of the Raipur Medical College where they were undertaken alkaline haemoglobin electrophoresis to distinguish the sickle cell trait from sickle cell disease. In the studied population 10.18% of the population are suffering from this genetic disorder, out of which, sickle cell trait (AS-9.9%) and diseases (SS-0.28%). Although the sickle cell trait occurred in all sections of Indian society, it was more common among the Scheduled Tribes and Other

backward class (OBC). The gene frequency data were not in Hardy- Weinberg equilibrium most readily accounted for by a deficiency of the SS phenotype who failed to enter the samples population, through either sickness or early death. All subjects with abnormal haemoglobin received permanent cards bearing personal information and haemoglobin genotype along with personal counselling and educational materials written in Hindi. It is hoped that those with abnormal haemoglobin genotype may factor this information into decisions regarding marriage and avoid the risks of having children with sickle cell disease.

7. **Profiling Î² Thalassemia Mutations in Consanguinity and Nonconsanguinity for Prenatal Screening and Awareness Programme**

   2015

   Advances in Hematology

   Kumar, Ravindra and Arya, Vandana and Agarwal, Sarita

Mutation spectrum varies significantly in different parts and different ethnic groups of India. Social factors such as preference to marry within the community and among 1st degree relatives (consanguinity) play an important role in impeding the gene pool of the disease within the community and so in society by and large. The present paper discusses the role of consanguinity in profiling of beta thalassemia mutation, and thus the approach for prenatal screening and prevention based awareness programme. Clinically diagnosed 516 cases of beta thalassemia were screened at molecular level. A detailed clinical Proforma was recorded with the information of origin of the family, ethnicity, and consanguinity. The present study reports that subjects originating from Uttar Pradesh, Uttarakhand, Bihar, and Jharkhand have c.92+5G>C and c.124_127delTTCT mutation as the commonest mutation compared to the subjects hailing from Madhya Pradesh and Chhattisgarh and Nepal where sickle mutation was found more common. In 40 consanguineous unions more common and specific beta mutations with higher rate of homozygosity have been reported. This consanguinity-based data helps not only in deciding target oriented prenatal diagnostic strategies but also in objective based awareness programmes in prevention of thalassemia major birth.

8. **Genetic counselling in tribals in India**

   2011

   Indian Journal of Medical Research

   Mohanty, D and Das, K

Genetic counselling in tribals unlike general population residing in cities and near villages is a difficult task due of their lower literacy and poor socio-economic status. However, sustained effort is essential with a close interaction in the local language, certain misbeliefs need to be removed gradually taking into account their socio-cultural background. The present communication deals with our experience in counselling for haemoglobinopathies during Neonatal Screening Programme undertaken for sickle cell disease in Kalahandi district of Orissa and Community Screening Programmes in primitive tribes of India in four States viz. Orissa, Gujarat, Tamil Nadu and Maharashtra. Counselling during neonatal screening programme was very well accepted demonstrating the benefit to the small babies as regards the morbidity. Premarital marriage counselling was also accepted by them. The success rate as followed up for 5 years is almost 50 per cent, the limitation being long follow up. Genetic counselling in these areas has to be continuous to achieve success and therefore the need for setting up of permanent centres in the tribal areas in India.

9. **Burden & pattern of illnesses among the tribal communities in central india: A report from a community health programme**

   2015

   Indian Journal of Medical Research, Supplement

   Jain, Y and Kataria, R and Patil, S and Kadam, S and Kataria, A and Jain, R and Kurbude, R and Shinde, S

Tribals are the most marginalised social category in the country and there is little and scattered information on the actual burden and pattern of illnesses they suffer from. This study provides information on burden and pattern of diseases among tribals, and whether these can be linked to their nutritional status, especially in particularly vulnerable tribal groups (PVTG) seen at a community health programme being run in the tribal areas of chhattisgarh and Madhya Pradesh States of India. This community based programme, known as Jan Swasthya Sahyog (JSS) has been serving people in over 2500 villages in rural central India. It was found that the tribals had significantly higher proportion of all tuberculosis, sputum positive tuberculosis, severe hypertension, illnesses that require major surgery as a primary therapeutic intervention and cancers than non tribals. The proportions of people with rheumatic heart disease, sickle cell disease and epilepsy were not significantly different between different social groups. Nutritional levels of tribals were poor. Tribals in central India suffer a disproportionate burden of both communicable and non communicable diseases amidst worrisome levels of undernutrition. There is a need for universal health coverage with preferential care for the tribals, especially those belonging to the PVTG. Further, the high level of undernutrition demands a more augmented and universal Public Distribution System.

10. **NIH recognizes sickle cell disease awareness month.**

    2010

    National Institutes of Health (NIH) Documents / FIND

11. **Initial outcomes of a comprehensive care-model for patients with sickle cell disease in a tribal population in rural Western India**

    2016

    Annals of Global Health

    Banerjee, S and Dave, K and Desai, G and Babaria, P and Gupta, R

Program Purpose: Sickle cell disease (SCD) is the most prevalent worldwide-inherited blood disorder, and is increasingly recognized as a neglected chronic disease. India claims 15% of the worlds' neonates born with SCD every year. Several cost-effective interventions have dramatically reduced morbidity and mortality from sickle cell disease in the US. However, access to care for SCD is unavailable in most rural tribal regions with the highest SCD prevalence in India. In 2014, we implemented a comprehensive care model at SEWA Rural, a non-profit health and development organization in Gujarat, India, with the aim of providing high quality comprehensive screening and treatment for sickle cell disease. Methods: Since 1980, SEWA Rural has operated the local public health care delivery system in partnership with the Government of Gujarat, including a 100-bed hospital with robust outpatient care system and community health worker model. In 2014, we implemented a comprehensive sickle cell treatment program. Components of the intervention include: universal newborn, antenatal and family screening; outpatient sickle cell clinic with pneumococcal vaccination, penicillin prophylaxis, and hydroxyurea for severe SCD; inpatient protocols for SCD crises; chronic disease registry with longitudinal population management; and health education and outreach via sickle cell health worker. Outcome and Evaluation: In 2014 alone, 7832 patients were screened for SCD in SEWA Rural with 176 patients being diagnosed with SCD. Since

February 2014, 370 SCD patients have been enrolled into the comprehensive care program to date. Of the 182 SCD patients followed for one year after enrollment, 134 (73.6%) of patients received pneumococcal vaccination, 8 (44.4%) of children under five were taking penicillin prophylaxis, and 128 (70%) were taking folic acid supplementation. Also, 23 (15.5%) patients had SCD crises, 21 (11.5%) were hospitalized, 10 (5.5%) received blood transfusions, and 3 died. Going Forward: This study demonstrates acceptability and feasibility of implementing a continuity care model for sickle cell disease in rural India. Further research is needed to evaluate the impact of the comprehensive sickle cell program on clinical and quality of life outcomes and retention in care.

12. **A comprehensive screening program for Î²-thalassemia and other hemoglobinopathies in the Hooghly District of West Bengal, India, dealing with 21 137 cases**

    2016

    Hemoglobin

    Bhattacharyya, K K and Chatterjee, T and Mondal, U B

We here present a report of population screening programs (January 2012â€“December 2015) conducted by the Thalassemia Control Unit, Imambara Sadar Hospital, Chinsurah, Hooghly in the Hooghly District of West Bengal, India for prevention of thalassemia. We screened Î²-thalassemia (Î²-thal) heterozygotes and homozygotes, and Hb E (HBB: c.79G > A)-Î²-thal compound heterozygotes. Among 21 137 cases, we found 1968 heterozygotes and 192 homozygotes or compound heterozygotes. Results were evaluated with standard hematological analyses including red cell indices, hemoglobin (Hb) typing and quantification. The participants of the screening program were divided into six groups (children, pre-marriage cases, post-marital cases, family members of affected individuals, family members of carriers and pregnant women). While considering the average frequency of carriers, many reports recorded both related individuals (family members of trait and affected individuals) as well as unrelated individuals such as school children and pregnant women. These would have to be considered separately and only the unrelated individuals taken to estimate carrier frequencies in this article that would give more realistic data on carrier frequency of unrelated individuals.

OTHERS

1. **Splenectomy in sickle cell disease.**

   1999

   The Journal of the Association of Physicians of India

   Kar, B C

INTRODUCTION: Since role of splenectomy in sickle cell disease still remains controversial, this paper evaluates the same in 32 cases of splenectomy in sickle disease patients observed by the author. MATERIAL AND METHODS: After proper diagnosis by standard methods the cases were observed for 2-3 years before deciding on splenectomy. Though acute splenic sequestration (53%) and chronic hypersplenism (21.8%) were the main indication. Two cases of splenic abscess and one case with frequent pain attacks were also subjected to splenectomy. There was one immediate post-operative death. RESULTS: The cases were followed up for 1 to > 8 years. While Acute splenic sequestration disappeared, in chronic hypersplenism cases as well as others besides a sense of general well being, steady state hemoglobin rose by > 2G/dl in 81% and significant increase in height and weight was seen in 90% and 61% cases respectively. Frequency of pain attack, fever, anaemia and need for blood transfusion improved in 79% patients. CONCLUSION: Splenectomy in selected cases appears to be an acceptable procedure in sickle disease.

2. **Study of risk factors and pattern of stroke in young adults (15 - 45 years) in a tertiary care hospital of Eastern India**

   2016

   Annals of Indian Academy of Neurology

   Sahoo, L K and Mallick, A K and Mohanty, G and Swain, K P and Nayak, S D and Samanta, M

Background: Stroke is the one of the most common cause of morbidity and mortality in India. Stroke in young adults can have a significant impact and long term burden on the patients, their families and the community in general. Objective: To study the risk factors and pattern of stroke in young adults. Materials and Methods: This is a prospective study conducted in Neurology Department of SCB Medical College, Cuttack, Odisha from September 2014 to June 2016. Stroke patients in age group between 15 and 45 years were evaluated by routine clinical examination, risk factors, neuroimaging, routine hematological and cardiological examination. A total of 52 patients were included. Results: There was female preponderance (60%). Mean age was 37.5} 7.9 years. Ischemic stroke was most common in 22 (42.3%) cases followed by hemorrhagic stroke in 20 (38.5 %) cases and cardioembolic stroke in 10 (19.2%) cases. Anterior circulation stroke was detected in 38 (73.1%) cases and posterior circulation stroke in 11 (21.2%) cases. Stroke involving both anterior and posterior circulation was seen in 1 patient and primary IVH in 2 patients. Single risk factor was present in 23 (44.2%) cases. Two risk factors were present in 13 (25%) cases and â‰¥3 risk factors in 3 (5.8%) patients. No risk factor was detected in 13 (25%) patients. Hypertension was the most common risk factor in 22 (42.3%) patients followed by diabetes mellitus in 11 (21.2%) patients. Among other risk factors valvular heart disease in 9 (17%) patients, dyslipidemia in 8 (15.4%) patients, coronary artery disease in 1 patient, vasculitis in 3 patients, sickle cell disease in 1 patient, chronic ITP in 1 patient and hyperhomocystinemia in 2 patients. Smoking and alcohol addiction was present in 2 patients each. The mean NIHSS score at admission was 12.4 Â± 5.7. The mean MRS score at admission was 4.52 Â± 1.0 and at discharge was 3.42 Â± 1.4. Two of the patients died during hospitalization. Conclusion: The present study indicates that hypertension is the most common risk factor of young stroke followed by diabetes mellitus and valvular heart disease. So special attention should be given for primary prevention of hypertension and diabetes mellitus.

3. **A Profile of Sickle Cell Status in a Hospital Based Sickle Cell Screening Programme of Bhilai Chhattisgarh**

2013

Thalassemia Reports

Meraj, F and Ravindranath, M and Singh, G and Bhaisare, R and Kango, M and Bhalla, M

Introduction: Bhilai is an Industrial township and has a multispecialty hospital providing health-care to a diverse population to people in and around Bhilai. The Jawaharlal Nehru Hospital and Research Centre Bhilai is a referral centre of Bhilai Steel Plant, which serve the employees of the same and other people also. Aim: i) To screen the patients of JLNH&RC for Haemoglobinopathies; ii) to analyse the trend of Haemoglobinopathies in Bhilai; iii) to educate the carriers and patients of Haemoglobinopathies accordingly. Materials and Methods: The present study was carried out over a period of one year (2011-2012) at Haematology laboratory of Pathology department of JLN Hospital and Research Centre. Twelve hundred ninety patients from paediatric and adult age groups were screened by solubility test. CBC, red blood cell indices, peripheral blood examination was done in all cases using the standard techniques. In abnormal cases family studies were carried out wherever possible. Blood specimens were collected in EDTA vials. All specimens were assessed by Bio-Rad Variant HPLC System, with the use of Variant Î²-Thalassemia Short Program Recorder Pack (Bio-Rad Laboratories). Results: Overall 220 families were screened and 1290 samples were tested. Sickle cell trait was detected in 37% Non com of cases, sickle cell disease in 3.8% and combination of sickle disease with thalassemia was observed in 8.7% of case. The trait and disease were equally seen in both the sexes. The average members in the family were found to be 4.5. Nearly 30% of the people screened were unaware that they were carriers of Sickle cell gene and were ignorant about the disease. Conclusions: Sickle cell trait is prevalent in and around Bhilai. Significant numbers of people were not aware of their sickle cell status. Efforts have to be initiated to educate the population.

4. **Risk factors associated with cerebro-vascular accident ischemic stroke in young and elderly population**

2020

International Journal of Pharma and Bio Sciences

Srikanth, S and Shulamite, B N and Mohan, C V and Reddy, K S and Kaveri, S

Cerebral ischemic stroke is caused by a blockage in a artery that supplies blood to the brain. The blockage reduces the blood flow and oxygen to the brain leading to the damage or death of brain cells. Aim of our study is to identify and analyze the risk factors of cerebral ischemic stroke in young and elderly patients. The known Non modifiable risk factors are Age, Gender, Race,, Family history of stroke, Low birth weight. Modifiable and well documented risk facrors are Hypertension, Sickle cell disease, Atrial fibrillation symptomatic carotid stenosis, Diabetes, Post menopausal hormone therapy, Dyslipidemia. Life style factors-associated with stroke risk Cigarette smoking, Obesity, Over Alcohol consumption, Physical inactivity. Potentially modifiable but less documented risk factors are usage of Oral contraceptives, Migraine,, Drug and alcohol abuse,, Homocysteine condition, Sleep disordered breathing. A Prospective observational study on risk factors of cerebral ischemic stroke in young and elderly patients was performed from September 2018-February 2019 i.e for 6 months duration in In-patient department of General Medicine in Gandhi Hospital.140 CVA cases were collected, documented, analyzed and results are obtained as follows. Young subjects HTN (60.9%), Alcohol consumption (78%), Smoking (48%), History of stroke (36%), Diabetes mellitus (24%), Obesity (14.6%), Cardio-Vascular diseases (4.8%). Elderly subjects HTN (82.8%), Smoking (79%), Alcohol consumption (72.7), History of stroke (33.3%), Diabetes mellitus (27.2), Obesity (8.8%), Cardio-Vascular diseases (8%). Reporting of Stroke cases in young adults in India was uncommon in few years ago. But our studies now indicate that the incidence of young stroke is on the rise. It has been observed that for the past 4-5 years the occurrence of stroke is seen at age less than 45years.And lifestyle modifications can reduce the rate of risk.

5. **Influence of sickle hemoglobinopahties on growth & development**

2010

Medico-Legal Update

Barmate, N D and Wakode, S L and Fulpatil, M P

Sickle cell anemia patients have acute and chronic vaso-oclusion which may lead to poor nutritional status, lower hematocreit, more marrow, cardiovascular compensation and combinations of these factors affect growth which is consistent with constitutional delay. Sickle cell syndrome has considerable effect over development of an individual there by affecting forensic age determination. The present project was undertaken to study the effect of sickle cell anemia on growth status of 120 (27 homozygous SS disease & 93 AS trait) children of sickle cell anemia & 122 normal school children. Age of subjects ranges from 5-20 yrs. The anthropometric parameters used were height, sitting height, length of hand, length of foot, interacromial & intercristal diameter. All measurements were taken in centimeters. Instruments used were antropometer & spreading calipers, weight was measured in kilograms. Calculated values were tested for statistical significance. Sickle cell anemic patients appeared to be significantly shorter & weight was significantly reduced as compared to control. Length of hand & foot shows significantly lower value as compared to control, interacromial & intercristal diameter was significantly less as compared to control. It can be concluded from present study that the growth of sickle cell anemic children is definitely affected by the disease process, children with sickle anemia are shorter, weigh less & have less transverse diameters. Therefore while examining a person for age assessment the forensic expert should address such issue and opinion should be furnished accordingly.

6. **Evaluation of Bone Mineral Density In Patients with transfusion dependent anemias**

2018

Pediatric Hematology Oncology Journal

Borkar, R and D'Sa, L and Silveira, M

Objectives: This study was conducted to assess Bone mineral density (BMD) in patients with Transfusion Dependent anemias that included Beta Thalassemia major, intermedia, Sickle beta thalassemia and Diamond Blackfan anemia; and to correlate the findings with biochemical and hematological profile of the patient. Materials & Methods: BMD in 23 patients with transfusion dependent anemias was calculated using Dual Energy Xray Absorptiometry technique at Lumbar Spine and Femoral Neck to see the prevalence of Osteopenia (Z score between -1.1 to -2.5) and Osteoporosis (Z score <-2.5) among adolescent patients, with transfusion dependant anemias. The effects of Serum calcium, phosphorus, alkaline phosphatase, ferritin, Vitamin D and Parathyroid Hormone on BMD was evaluated using the SPSS software version 14. Results:BMD results of 23 adolescent children were evaluated with ages ranging from 13 years to 24 years. There were 14 males and 9 females. 16 children were diagnosed as Beta Thalassemia major, 3 were thalassemia intermedia, 2 sickle thalassemia, and 1 each of Diamond blackfan syndrome and non-thalassemic transfusion dependant anemia. 6 patients had DEXA Z score values less than -1 i.e. normal BMD when measured at Lumbar spine, while 1 patient had normal BMD when measured at femoral neck. 9 patients were found to be osteopenic when BMD was measured at lumbar spine, while 4 patients were found to be osteopenic when BMD was measured at Femoral Neck. 8 patients were found to have Osteoporosis when BMD was measured at Lumbar spine while 2 were found to have osteoporosis when measured at Femoral neck. Conclusion: It was observed that BMD at Femoral neck had significant correlation with serum ferritin & Vitamin D levels. The same correlation was however not observed at Lumbar spine. Other parameters were not observed to have any effect on the BMD. References 1. Mehran Karimi et al. Bone mineral density in beta thalassemia major and intermedia. Indian Pediatrics 2007; vol 44: 29-32

7. **Quality of life in children with sickle cell hemoglobinopathy**

   2005

   Indian Journal of Pediatrics

   Patel, A B and Pathan, H G

Objective: To identify specific domains and traits that are most affected in patients with sickle cell anemia and traits with respect to normal children. Methods: Children attending the regional hemoglobinopathy center at IGMC, Nagpur in age group of 8-14 years were assessed. Of 52 children studied, 25 had sickle cell anemia (SCA), 12 had sickle cell trait (SCT) and 15 wre normal control. The (quality of life (QOL) was assessed using multidimensional interview based questionnaire. Results: All domains, physical, psychosocial, cognitive and morbidity were affected. In SCA playing and mobility were most affected. There was feeling of sadness or disinterest and lack of support from teachers. The school attendance, vocational achievement perception, entertainment and participation in cultural activities were also affected. The intensity of weakness and pain was greater in SCA children who left that they were affected by a major illness. The unusual finding was that the SCT children also showed affection of all domains as compared to normal children, which was perhaps due to the stigma of the disease. Conclusion: QOL is affected in children with sickle cell disease (SCD) and to a lesser extent in SCT. Interventions to improve QOL should target the affected items. Improving awareness of the disease and its manifestation will help to alleviate the psychosocial affliction of children with SCT.

8. **Sickle Hepatopathy. uncommon Presentation of Infrequent Complication**

   2013

   Thalassemia Reports

   Poornima, D R and Karuna, R K and Parimala, P and Prakash, A

Introduction: Intrahepatic sequestration is an uncommon complication of sickle cell disease and occurs in homozygous sickle cell anemia. Case Reports: case #1: A 7-year old boy (non consanguineous marriage, sibling not affected) presented with fever of 5 days duration. On examination, he was very pale, icteric, had hepato splenomegaly (7 cm below costal margin) and lymphadenpathy. 8 months back had a similar episode with history of blood transfusion. 10-year old sibling is asymptomatic. Significant laboratory results: haemoglobin: 3 gm%. Corrected total count 22,800/Î¼L corrected reticulocyte count: 7.75% high conjugated hyper bilirubinemia; enzymes not elevated, smear for malaria was negative. case #2: A 5-year old boy (consanguineous marriage, sibling with H/o blood transfusion) presented with fever of 5 days duration. H/o transfusion of 3 years back. On examination, pale, icteric and had hepatosplenomegaly (4 cm below the costal margin). Significant laboratory results: haemoglobin: 8.9 g/dL; conjugated hyperbilirubinemia (12.8/10.8); enzymes elevated (608/255); reticulocyte count: 1.75%. HPLC done on both patients showed features of sickle cell-Î² thalasemia. Both patients did not have gallstones on ultrasound evaluation. Conclusions: Sickle cell anemia usually presents with mild splenomegaly and unconjugated hyperbilirubinemia. Acute sickle hepatic crisis occurs in approximately 10% of patients with sickle cell anemia and relate predominantly to vascular occlusion with acute ischemia and sequestration. These two cases with hepatosplenomegaly and conjugated bilirubinemia highlight the varied presentation of sickle hepatopathy in these patients with sickle-Î²-thalassemia.

9. **Study of placenta in sickle cell disorders**

   2007

   Indian Journal of Pathology and Microbiology

   Rathod, K B and Jaiswal, K N and Shrivastava, A C and Shrikhande, A V

Remarkable changes are seen on gross and microscopic examination of placenta of patients with sickle cell disorders, hence the present study was undertaken to find out the pathological changes seen in the placenta of sickle cell disorder patients, as compared to control and to study the effect of maternal sickling on the fetus. It includes total 73 cases, of which 10 were of control group and 63 were from patients with sickle cell disorders, which included 47 sickle cell trait (AS) and 16 sickle cell disease (SS) patients. In group II, 9(14.28%) patients with SS pattern developed complications during pregnancy, in the form of vaso-occlusive and hemolytic crises. Pregnancy induced hypertension was seen in 4(25%) out of 16 SS and 11(23.40%) of the 47 AS patients. Urinary tract infection(UTI) was seen in 6(37.5%) out of 16 SS and 8(17.02%) out of 47 AS patients. Placentae in sickle cell disorders showed pathological changes in the form of infarction, calcification, sickled red blood cells and hemorrhage in intervillous spaces, increased syncytial knots, fibrinoid necrosis, stromal fibrosis, hyalinised villi and compensatory proliferation of trophoblastic cells.

10. **Fetal hemoglobin & liver dysfunction in sickle cell crisis**

    2011

    Indian Journal of Public Health Research and Development

    Panigrahi, S and Sablania, P and Khodiar, P K and Keshari, J R and Patra, P K

Fetal hemoglobin is one of the major factors that alters the clinical course of disease. A study of 45 patients of sickle cell crisis was carried out in Department of Biochemistry & Department of Pediatrics, Pt JNM Medical College, Raipur, Chhattisgarh between June 2007 to July 2009. All patients had homozygous sickle cell anemia admitted in our institutional hospital for sickle cell crisis. Patients were diagnosed by cellulose acetate electrophoresis and adult, fetal and sickle hemoglobin was quantitated by cation exchange HPLC (Biorad Variant hemoglobin testing system). The patients were divided into three groups based on the Hb F concentration in whole blood. Group I, II and III had <10, 10-20 &>20 percent HbF respectively. HbF is higher in lesser age group but it was not statistically significant. The average Sickle cell crisis per year and recurrent events were 2.7, 3.2 and 1.4 in group-I, group-II and group-III respectively. So in group-III the crisis/year was less than compared to other two groups. The average number of blood transfusions in groups I, II & III till the study period was 14, 7.1 and 3.1 respectively. So there was a downward trend of no. of B.T with increasing level of HbF. There was significant drop in the requirement of B.T, reccurence of sickle cell crisis in the patients above HbF level of 20%. The mean size in centimeters of spleen was lower with increasing HbF level. but there was no significant difference in liver size. SGOT & SGPT was in normal reference range in patients with HbF level > 20% whereas it was abnormal in patients with HbF levels < 20%. There was no significant difference in hematological parameters like Hb, MCV, HCT, RBC, MCH & MCHC between any of the groups. However platelet count was elevated with HbF levels < 20% and in normal range with HbF levels > 20%.

11. **Determination of allelic frequency of SNPS at quantitative trait loci (QTL)s of fetal hemoglobin**

    2012

    Indian Journal of Hematology and Blood Transfusion

    Batra, C and Kaur, J and Trehan, A and Ahluwalia, J and Das, R

Introduction: Fetal Hemoglobin (HbF) is considered a 'quantitative trait' (QT) wherein multiple genes together with a small environmental component determine the value measured in any given individual. High HbF levels are associated with milder disease progression and fewer complications in patients with Sickle cell Disease (SCD) and Î² thalassemia. Recently conducted Genome-Wide Association Studies (GWAS) in European and African American populations and patients with hemoglobinopathies, have identified single-nucleotide polymorphisms (SNPs) from chromosomal loci that contribute to varying expression levels of HbF and other clinical traits. They include the Xmn1-GÎ³ polymorphism and SNPs at BCL11A and HBSB1L-cMYB inter-region loci. To the best of our knowledge, the allelic frequency of SNPs at BCL11A and HBS1L-MYB intergenic region in normal North Indian population and their association with thalassemia in India has not been studied. Objective: Determination

of prevalence of polymorphism at SNP rs11886868 in BCL11A exon 2, SNP rs4895441 in the HBSB1L-cMYB inter-region and SNP rs74822144 in Î² globin gene cluster (The Xmn1-GÎ³ polymorphism) in normal North Indian population. Methods: Single-nucleotide polymorphism (SNP) analysis was performed by using polymerase chain reaction (PCR)/restriction enzymes on genomic DNA extracted from peripheral blood leukocytes of fifty healthy normal children>3 years of age. Enzymatic digestion was performed by XmnI, MboII, and RsaI for, rs74822144, rs11886868 and rs4895441 respectively. Results: Minor allele frequencies for rs11886868 and rs4895441, rs74822144 were 0.35, 0.13 and 0.26 in normal North Indian children. We plan to determine the allelic frequency at these loci in children with thalassemia intermedia and to correlate the SNPs with the clinical phenotypes.

12. **A comparative study of 24 hours ambulatory blood pressure (ABPM), renal function and proteinuria in children with sickle cell disease**

    2016

    Pediatric Nephrology

Bhatt, G C and Shrivastava, N and Dubey, S R K and Goel, S K and Tanya, S and Dhingra, B and Joshi, D

Objectives To measure24 hours ambulatory blood pressure through ABPM, proteinuria, glomerular filtration and renal function in Sickle cell disease(SCD) with normal controls. b. Methods Fifteen children diagnosed with SCD and nine healthy controls were included in this study. After taking informed consent from all participants, both the groups underwent renal function, urine specific gravity and proteinuria (UP/UC spot) assessment. In both the groups three resting BP measurements were obtained from the right upper arm using an aneroid sphygmomanometer with appropriately sized cuff. For assessment and comparison of diurnal blood pressure variation in cases and controls both the groups underwent ABPM for 24 hours with appropriate size cuff c. Results 15 patients and 09 controls were enrolled for the study. Baseline characteristics of the two groups were similar. Office BP revealed pre-hypertension in two subjects with SCD. White coat hypertension was present in two subjects in the control (22.2%). Ambulatory blood pressure in SCD revealed lower 24 hours mean systolic BP(95.4Â±9.8 vs 97.8Â±7.2,p=0.523);24 hours mean diastolic(56.8Â±8 vs 59.0Â±2.7); daytime systolic BP averages(97.7Â±9 vs 100.3Â±7.7); daytime diastolic BP averages(58.1Â±8.1 vs 1.0Â±3.4);nighttime systolic BP averages(85.6 Â±13.7 vs 90.7Â±6.8) and nighttime diastolic averages(48.8Â±9.8 vs 53.4 Â±2.8) Abnormal dipping pattern was high in the patients with sickle cell disease(7/15 vs 1/9,p=0.04). GFR was abnormally high in SCD patients as compared to controls (210.2Â±60.1 vs 154.2Â±48.3,p=0.027) and hyper- filtration(GFR >140ml/min/1.73m2) was found in all SCD and 3 controls, p<0.001. Also, lower value of serum creatinine was observed in patients of SCD(0.29Â±0.10 vs 0.40Â±0.17,p=0.03) d. Conclusions Abnormal dipping pattern was found in patients with SCD, thus implicating a high risk of cardiovascular abnormality in these patients. Moreover, lower ABPM values, hyperfiltration and low creatinine were more common in SCD patients as compared to controls.

13. **Prevention and management of alloimmunization by establishment of extended red cell phenotype voluntary donors data base in tertiary care hospital: A distant vision**

    2016

    Vox Sanguinis

    Bajpayee, A and Kaur, A

Background: The well-known risks associated with repeated transfusions include alloimmunization and increased donor exposure. The use of extended red blood cell (RBC) antigen matching has been well documented in reducing alloimmunization. The knowledge of RBC antigen phenotype frequencies in a local population is helpful in terms of their ethnic distribution, when dealing with patients dependent on chronic transfusion therapy and who have developed multiple alloantibody. Registry of extended red cell antigen phenotyping in repeat voluntary donors can create a credible database of antigen- negative donors for patients having clinically significant irregular

antibodies and phenotype match transfusion program in thalassemics and sickle cell disease patients. Aims: The present study was conducted to create a voluntary donors data base of young donors of known clinically significant minor blood group antigens, to provide extended antigen phenotype match blood to local patient population of thalassemia and sickle cell disease. To provide antigen negative blood for patients having multiple antibodies in emergency. Material and Methods: The prospective study was conducted in AIIMS,Jodhpur from Dec'14 to Mar'16. The KAP (knowledge, attitude and practice regarding voluntary blood donation) study was conducted in local population. From the participants of the KAP study prospective regular voluntary donors of group O were identified by ABO grouping and extended antigen phenotyping for RBC antigens was done in these donors for antigens D, C, c, E, e, K, Fya, Fyb , Jka , Jkb , M, N, S & s status by serologic methods using tube method and Gel cards (Diamed, Switzerland). Results: Out of 1000 participants of KAP study, 200 young (18-25 yrs of age) â€œGroup Oâ€voluntary donors were recruited for RBC antigen phenotyping. The antigen frequency among Rh blood group system was found to be D (92.2%), C (84.2%), c (62.3%), E (23.7%) and e (98.2%). Within the MNS blood group system, antigen frequency was M (89.5%), N (51.7%), S (64%), and s (78.7%) and in the Duffy blood group system, antigen frequency was Fya (87.7%) and Fyb (51.7%). The antigen frequency for Jka and Jkb was 81.6% and 50% respectively. Among 200 donors we listed 18 C neg, 21 Jka neg, 12 M neg and 14 Fya neg donors and reserved these donors for those patients who need antigen negative units due to alloantibodies. The newly registered thalassemia and sickle cell anemia patients were phenotyped for minor RBC antigens and we made a registry of minor RBC antigen matched donors for each patient. This strategy helps us to bleed these clinically significant minor antigen typed donors on the base of our requirement. Conclusion: The Apex centers of the country that hold up chronic transfusion therapy in transfusion dependent patients, should maintain extended red cell phenotype voluntary donors data base in a software where antigen negative donors can be found on one click. It could be helpful in cases of emergency and complex cases of multiple alloantibodies. Phenotype matched transfusion in thalassemia and sickle cell anemia can largely reduce the problem of alloimmunisation and incompatible cross-match.

14. **Case series of HbQ-India, a rare alpha globin variant in a referral laboratory setting in South India**

2020

Indian Journal of Pathology and Microbiology

Shaik, A and Thekkelakayil, S and Kumawat, V and Gupta, A and Goyal, M

HbQ variants are rare alpha globin chain variants commonly found in Sindhi community. It results from a point mutation of Î±-1 globin gene at position 223 of the coding region of exon 64. It is inherited in an autosomal dominant fashion. HbQ-India is usually clinically silent in heterozygous state unless associated with other conditions like beta thalassemia, alpha thalassemia, HbE disease, or nutritional anemia. High performance liquid chromatography (HPLC) identifies HbQ-India with a prominent peak present just after the Sickle window. We present five cases of HbQ-India from a retrospective analysis of 6034 cases over a period of 3 years, a rarity in a referral setting of South India. Awareness of this entity is important for appropriate recognition to prevent clinically symptomatic hemoglobinopathies. This study also highlights the retention time (RT) and characteristic chromatographic HPLC pattern seen in HbQ-India.

15. **Spectrum of Sickle Cell Disease in Patients Diagnosed at Indira Gandhi Institute of Child Health along with their Family Screening and Special Emphasis on Clinico-Hematological Profile of Patients**

2013

Thalassemia Reports

Hemalata, L and Pradeep, R and Premalatha, R and Viswanath, V and Murthy, G R

Introduction: Sickle cell anemia is the most common heritable hematological disease affecting humans. Because of their prevalence and worldwide distribution, disorders resulting from sickle haemoglobin are of enormous clinical importance. Aim: The aim of this study was to identify the spectrum of all sickle cell diseases diagnosed at Indira Gandhi Institute of Child Health, Bangalore and to screen parents and siblings of the patients for their carrier status. Materials and Methods: 26 children diagnosed to have sickle cell disease over a period of five years (2008 to 2012) from inpatient and outpatient departments of IGICH, Bangalore were studied. 38 Parents and 10 siblings of these children were studied for their carrier status. Standard methods were used for routine hematological and biochemical investigations. Hemoglobin electrophoresis was done by alkaline gel method. Results: Age of the children ranged from 1 Â½ years to 14 years. 12 out of 26 children presented in hemolytic crisis, one child presented in aplastic crisis and the others presented with constitutional symptoms. 11 out of 26 children were diagnosed with sickle cell anemia, 8 were diagnosed with sickle thalassemia and 7 were diagnosed with sickle cell trait. Among the parents and siblings, 40 were found to have sickle cell trait, 7 were found to have thalassemia trait and one was electrophoretically normal. Conclusions: Sickle cell anemia was the most common sickle cell disease in the patients followed by sickle thalassemia and then sickle cell trait. Sickle cell trait was the most common entity among the parents and siblings, followed by thalassemia trait.

16. **Bone marrow necrosis: A retrospective analysis of an uncommon entity**

    2011

    Indian Journal of Hematology and Blood Transfusion

    Uthamalingam, P and Naseem, S and Sachdeva, M and Ahluwalia, J and Das, R and Verma, N

Background: Bone marrow necrosis (BMN) is an uncommon finding. It is seen in patients with neoplastic disorders, severe infections and sickle cell anemia. This study was undertaken to evaluate the incidence of BMN and the clinico-hematological profile in cases with BMN. Materials & Methods: All bone marrows performed from January 2009 to July 2011, in the Hematology department, PGIMER, were retrospectively reviewed. Records of cases showing BMN were retrieved and detailed clinical and laboratory findings recorded. Results: Of 6,147 bone marrow procedures performed during the study period, only 13 (0.2%) showed BMN, of which 7 were adults and 6 children. In 6 of the 7 adult patients showing BMN, it was the presenting feature and all but 1 (final diagnosis could not be made, as patient was lost to follow up) had underlying malignancy (acute leukemia in 2 cases and NHL in 3). In the pediatric group, BMN was the presenting feature in 2 cases, both had malignancy (NHL infiltration). Other 4 cases with BMN were known ALL patients on chemotherapy, 3 of which also showed mucinous degeneration and the other showed residual leukemia. All the patients with BMN had one or more cytopenias-anemia in 77%, thrombocytopenia in 70% and bicytopenia/pancytopenia in 54% cases. None of the cases except one showed blasts/atypical cells/leukoerythroblastic picture. Conclusion: BMN was found to be an infrequent finding in routine bone marrow biopsies in this study. All the cases were associated with malignancy and cytopenias. In the presence of BMN, degree of suspicion for an underlying malignancy should be kept high.

17. **Social perception about sickle cell disease and its prevention in unmarried tribal males of Gujarat**

    2009

    Biomedicine (India)

    Saxena, D and Shah, H and Bhardwaj, P and Jha, T

Sickle cell anemia is an important health problem frequently seen in tribal communities of Gujarat as well in India. It's an autosomal recessive disorder in which as a result of abnormal hemoglobinopathy leading to chronic hemolytic anemia with a variety degree of clinical consequences. The diagnosis is made clinically supported by laboratory investigations which define them as diseased (homozygous) and Traits (heterozygous). Present study aims at documentation of social perception and prevention of sickle cell anemia in tribal unmarried males of south Gujarat. Out of those who participated in the study 50% had heard about and out of those who had heard about SCA only 50% knew that it was a genetic disorder. Only one student out of those who participated in the study

had under taken screening test for SCA before the study, rest all though belonged to high risk tribal population had never undertaken screening test for SCA. Screening test with DTT & electrophoretic test was performed on the participants and after electrophortic test, three were detected positive for sickle cell disease whereas nine had sickle cell trait.

18. **Spectrum of haemoglobinopathies diagnosed by cation exchange-HPLC & modulating effects of nutritional deficiency anaemias from north India**

    2010

    Indian Journal of Medical Research

    Rao, S and Kar, R and Gupta, S K and Chopra, A and Saxena, R

Background & objectives: The usefulness of cation exchange high performance liquid chromatography (CE-HPLC) as a tool for detection of thalassaemia/haemoglobin variants was evaluated in a prospective study in a tertiary care centre in north India. We also tried to evaluate the effect of concurrent nutritional deficiency on the HPLC pattern in the local ethnic population.Methods: A total of 800 blood samples were analyzed on the Bio-Rad Variant HPLC system by Î²-thal short program. The retention times, proportion of the haemoglobin (%), and the peak characteristics for all haemoglobin fractions were recorded. Alkaline and acid haemoglobin electrophoresis was performed to document the identities of the haemoglobin variants, wherever necessary. Many cases were subjected to family studies for a definitive diagnosis.Results: Among 800 samples tested, 553 (69.1%) were found to have normal HPLC pattern. Apart from Î²- thalassaemia, nine additional variants were encountered; HbS (2.8%), HbE (2.5%) and HbD (1.1%) being the most common variants present. Other variants included Hb Q-India, Hb-Lepore, Î´Î²-thalassemia/ HPFH, HbD-Iran, HbJ-Meerut and HbH disease. There was a significant decrease in the level of HbA2 associated with iron deficiency anaemia (IDA) (P=0.004) and increase in megaloblastic anaemia (P<0.001) among subjects with normal HPLC pattern. Interpretation & conclusions: HPLC was found to be a simple, rapid and reliable method for the detection of hemoglobin variants. An accurate diagnosis can be provided in majority of cases by use of retention time, proportion of total haemoglobin, and peak characteristics of HPLC. Haemoglobin electrophoresis and family studies play a valuable role in difficult cases. Concurrent nutritional deficiency also has an effect on HbA2 levels.

19. **Natural history of sickle cell disease in central india: A retrospective analysis of 2 to 11 years**

    2010

    American Journal of Hematology

    Jain, D

Objective: Sickle Cell Anemia in India has a mild clinical presentation, is the common belief. However, it is not so in Central India, where they present with very severe manifestations. Hence there was a need for better information on the natural history of Sickle Cell Disease among patients residing in this part of the world. Design: Retrospective Cohort Subjects : A retrospectively study of 220 non- tribal sickle patients [Group I Birth-5 years - 84 patients, Group ll> 5-10 years - 99 patients Group III 10-15 years - 37 patients] was undertaken and these children were followed up regularly after diagnosis for an average of 4,0 + 2.6 years. Results: Severe Anemia was the most common manifestation seen in 69%, 74.7% and 86.5% of patient in group I, II and III respectively, Acute Painful event was seen in 42.8%, 45.4% and 48.6% of patients and severe infections in 16.6%, 20.2% and 8.1% of patient in group I, II, and III respectively 3.6% of the patient had stroke and 7 deaths accrued. Staph aureus and salmonella were common bacteria isolated. Conclusion: Sickle Cell disease patients residing in central India have a more severe clinical presentation. They form a large burden of illness on health system in Central India. Implication: A Prospective Cohort in which subject are recruited through Neonatal Screening Program is on going in our department. Results of this will be available at the line of presentation.

20. Genetics of fetal hemoglobin: Relevance for prognostication

2014

Indian Journal of Human Genetics

Bhanushali, A A and Patra, P K and Pradhan, S and Khanka, S and Nair, D and Singh, S and Verma, H and Das, B R

Background: Though SCD is a monogenic disorder, at the phenotypic level it is a multigenic disease, with different clinical outcomes. These variable outcomes could be attributed to genetic modifiers. Several studies have revealed fetal hemoglobin (HbF) as a major genetic modulator in SCD. Recently, Genome wide association studies have indicated three major quantitative trait loci; Xmn-HBG2, HBS1L-MYB intergenic region and BCL11A locus to account for 20-50% of the variation in HbF levels in SCD patients. Aims and Objectives: There is minimal information about genetic factors influencing the disease course in Indians. The current study is the one of the first report investigating genetic variants at these loci affecting HbF levels. Materials and Methods: The current study was conducted on 240 SCD and 60 sickle cell trait individuals. Genotyping was performed for the BCL11A rs11886868, rs1427407; HMIP rs9399137, rs6934903; HBG2 Xmn1 polymorphism rs7482144; -68 C>T HBD promoter polymorphism. Frequency and association of these variants with HbF levels was analyzed. Results: All the 3 loci were associated with HbF levels in Indian SCD patients. The BCL11A rs1427407 was significantly associated with HbF levels contributing to âˆ¼23% of the trait variance, the BCL11A rs11886868 for 3.65%, HMIP rs9399137 for 3.8% and XMN1 accounted for 11% of the trait variance. Interestingly no association of the HBS1L-MYB rs6934903 with the HbF levels was seen. This study also determines the presence of the promoter polymorphism -68C>T in the HBD gene which was exclusively seen in individuals with Arab-Indian haplotype and has hitherto been unreported in Indians. Conclusions: The present study indicates the BCL11A, HMIP and Î²-Globin region to be associated with elevated HbF levels. Further interrogation of these variants with respect to pain crisis is warranted, as they are also known to associate with pain crisis and hospitalization rates. This may aid in prognostication.

21. Sickle cell crisis-varied manifestations

2018

Indian Journal of Hematology and Blood Transfusion

Poulose, P and Kumar, J and Sajeevan, C and Sasidharan, P K

Aims & Objectives: INTRODUCTION Sickle cell disease is characterized by various life threatening crisis like Vaso occlusive crisis. hemolytic crisis , Sequestration crisis , Aplastic crisis. Patients/Materials & Methods: CASE SERIES CASE -1 17 yr old boy admitted with fever, jaundice, joint pains since 1 week. Multiple episodes of epistaxis, vomiting and malena post admission. HbSS +, Total /Direct bilirubin -71/30 , RMA-Positive, H63D Homozygous mutation positive. Diagnosis - Acute sickle cell hepatic crisis, Sickle cell intrahepatic cholestasis(SCIC), Cholelithiasis, Complicated malaria, Splenic abcess -Sepsis, Hypogonadotrophic hypogonadism, Hemochromatosis (Primary/Secondary) CASE-2 22 yrold male HbSS presented with headache. backache since 2 days. altered sensorium since 1 day. CT Brain -Bilateral Extradural hemorrhage. Diagnosis - Spontaneous Extradural Hemorrhage in Sickle cell disease CASE -3 19 yrold male with HbSS presented with acute onset flaccid areflexic quadriparesis with bilateral LMN facial palsy and bulbarweakness. Diagnosis - Guillain Barre syndrome in Sickle cell Disease CASE -4 34 yr old female HbSS with history of multiple transfusions. presented with severe anemia Hb-3.2 , Reticulocyte counts elevated. ICT -Positive. Not able to transfuse due to red cell alloimmunization. Showed good response to steroids. Diagnosis- Hyperhemolytic crisis CASE-5 35 yr old male from Wayanad presented with small bowel diarrhea. His RFT -Urea/Creat-127/4.3, LFT transaminases elevated SGOT /SGPT - 117/307. HUS workup negative. Sickling test positive. Sickle cell trait positive. Diagnosis- Hepatorenal syndrome -Due Vaso occlusive crisis CASE-6 20 yrold female Kuruma tribe presented with acute chestsyndrome , Day2 of admission had headache and proptosis of left eye. CT Orbit -Left Intraorbital hemorrhage. Diagnosis -Sickle cell crisis with Left intraorbital hemorrhage (Due to orbital wall infarction) CASE-7 25 yrold male HbSS with fever , cough , breathlessness. Sp02 -72%. Diagnosis -Acute Chest SyndromeCASE-8 33 yrold female HbSS Diagnosis -Multiple liverabcess. Splenic infarcts , Recurrentcholangitis. Results: 7 cases -Vaso occlusive crisis , 1 case -Hemolytic crisis Discussion & Conclusion: Prompt recognition

and aggressive treatment of sickle cell crisis needs to be advocated inorder to avoid increased morbidity and mortality.

22. **Emphysematous osteomyelitis caused by Salmonella typhi in beta thalassemia major**

    2019

    Journal of Postgraduate Medicine

    Doctor, P N and Verma, M and Varaiya, A and Merchant, R H

There have been various cases of salmonella osteomyelitis reported in sickle cell anemia. We present a case of emphysematous osteomyelitis caused by Salmonella typhi in a 29-year-old beta thalassemia major patient. Diagnosis of emphysematous osteomyelitis was confirmed by computed tomography and magnetic resonance imaging, and culture of pus drained during surgical debridement confirmed the causative microorganism, Salmonella typhi. Antimicrobials were given according to microbiological sensitivity for a period of 8 weeks. Our patient also received hyperbaric oxygen therapy. At the end of therapy, he was afebrile and laboratory parameters normalized with a residual joint deformity which developed within 3 months.

23. **Hematological manifestations of parvovirus B19 infection: Institutional experience**

    2009

    Indian Journal of Hematology and Blood Transfusion

    Singh, M and Gupta, P and Manda, S and Singh, T and Dubey, A P

Background: The characteristic bone marrow manifestation of Parvovirus B19 infection is presence of Giant Proerythroblast, which is pathognomonic of this infection. Serology as a diagnostic tool is not much reliable in immunocompromised patients. Aim: To study the hematological spectrum in cases of Parvovirus B19 infection. Materials and method: Over past 9 years 54 cases of parvovirus B19 infection were diagnosed based on presence of Giant Proerythroblast in the marrow. Serology was carried out only in doubtful cases. Follow-up was available for only 19 cases out of which 13 showed complete recovery. Result: Out of 54 cases, Immunodeficiency (26 cases) was the most common predisposing factor comprised predominantly of hematological malignancies on treatment (ALL -13, CLL-2 and Burkitt's lymphoma -1) followed by HIV positive cases (10). Other predisposing conditions were Hemolytic anemias (11; comprised of 4 Hereditary spherocytosis, 3 Sickle cell anaemias, 2 thalassemia and 2 autoimmune hemolytic anemia), nutritional deficiency (7), congenital dyserythropoetic anemia (3), protein energy malnutrition (3), tuberculosis (2), Gaucher's disease (1) with no data available in one. The manifestations included PRCA in 17 cases, red cell hypoplasia in 14, hypoplastic marrow in 9, aplastic anemia in 7, red cell hypoplasia with thrombocytopenia in 3, isolated thrombocytopenia with dysmegakaryopoesis in 2 (ITP), red cell hypoplasia with leucopenia in 2 with dysmyelopoesis in one of them. Associated marrow findings included Gelatinous Marrow transformation in 21, increased marrow lymphocytes in 13, plasmacytosis in 4, megakaryocytic hyperplasia in 2. Conclusion: Most common predisposing factor for B19 infection is immunodeficiency, and giant proerythroblast should be actively searched for in cases of red cell aplasia/hypoplasia with gelatinous marrow transformation.

24. **Evaluation of various hemoglobinopathies and thalassemia syndromes on high-performance liquid chromatography**

    2018

    Indian Journal of Pathology and Microbiology

    Ratnaparkhi, S R and Bhadarge, P and Agrawal, A and Chhadi, T and Pande, N P

Objectives: The aim of this study is to evaluate the diagnostic utility of high-performance liquid chromatography (HPLC) in various hemoglobinopathies and thalassemia syndromes. To correlate HPLC findings with the hematological profile of cases. Methods: A total of 3525 samples were screened for hemoglobinopathies on

solubility test and alkaline hemoglobin (Hb) electrophoresis. Out of these, samples from all cases of sickle cell anemia (SS), thalassemia (A2), other hemoglobinopathies, and family members of affected individuals were run on HPLC. Total of 337 blood samples was studied on the Bio-Rad Variant II HPLC system by the Î²-thal short program. Complete blood counts were also analyzed. Results: Among 337 samples, 42.14% were of SS, followed by AA (20.47%). Sickle cell trait (AS) and double heterozygous for sickle and thalassemia were each 9.20%. Other various hemoglobinopathies such as Hb J, Hb E, and Hb D trait were also detected. CBC parameters were also compared with each hemoglobinopathies. Conclusion: HPLC is found to be a simple, rapid, and precise method for the detection of Hb variants in areas with high prevalence of hemoglobinopathies like central India. Hematological parameters were found to be correlating with profile of respective hemoglobinopathies.

25. **The physical and social associations of common mental disorder in a tribal population in South India**

    2007

    Social Psychiatry and Psychiatric Epidemiology

    Hackett, Richard J and Sagdeo, Dhananjay and Creed, Francis H

Previous studies have shown high prevalence rates of Common Mental Disorder (CMD) in developing countries, however few have studied its relationship with physical morbidity. To examine the association between CMD and anaemia, malnutrition and physical symptoms. Outpatients attending a hospital for tribal people in Kerala, India were interviewed to collect information on demographic characteristics, physical symptoms and life events. They were weighed and measured and their haemoglobin concentration was measured. Associations between these data and Self Report Questionnaire (SRQ) score were examined. Multivariate analysis showed high SRQ score was associated with more physical symptoms, being female, no education and more life events in the past year. The main associations of CMD are social. The association with physical symptoms may also be socially mediated.

26. **Perioperative management of sickle cell disease in paediatric cardiac surgery**

    2007

    Anaesthesia and Intensive Care

    Bhatt, K and Cherian, S and Agarwal, R and Jose, S and Cherian, K M

In sickle cell disease, cardiopulmonary bypass may induce red cell sickling. Partial exchange transfusion reduces the circulating haemoglobin S level. We report the management of a child with sickle cell disease who required surgical closure of a ventricular septal defect. Preoperative exchange transfusion of 50% of the total blood volume was performed with fresh packed red cells over three days. Further exchange transfusion was performed as cardiopulmonary bypass commenced. The haemoglobin S level was reduced from 76% to 37%. The blood removed from the patient during the exchanges was processed allowing storage and re-infusion of the patient's plasma and platelets. Combined preoperative and intraoperative exchange transfusions, instead of a single stage 50% volume exchange, was effective and potentially avoids larger haemodynamic effects. Cardiopulmonary bypass was conducted at normothermia and cold cardioplegia was avoided (fibrillatory arrest was used during the surgical repair).

27. **Current, Emerging, and Anticipated Therapies for Sickle Cell Disease**

    2018

    Mayo Clinic Proceedings

    Nath MBChB, Karl A and Rajkumar MD, S Vincent

Sickle cell disease (SCD) is the most frequent monogenic disorder and hereditary hematologic disease worldwide.1-4 Currently afflicting well over 300,000 live births each year, such rates are expected to markedly increase in the years ahead.2,3 In its discovery, pathobiology, and therapeutic challenges, SCD stands entirely apart from any other known clinical disorder.1-4 Features of SCD have been recognized in Africa for centuries, and in the English literature, sickle red blood cells (RBCs) were first described in a West Indian student studying dentistry in Chicago who presented with fevers, pain, leg ulcers, jaundice, and pulmonary symptoms.5 Other case reports then documented the presence of such cells in similarly symptomatic patients, and the seminal observation was made that deprivation of oxygen ex vivo rapidly triggered the sickling of RBCs obtained from patients with this disease. Sickle cell disease ushered in the age of the molecular disease paradigm: in the of case of SCD, a DNA point mutation in the ÃŸs gene led to the substitution of a single amino acid (valine for glutamic acid) in ÃŸ-globin; this created a mutant hemoglobin protein (hemoglobin S [HbS]) prone to polymerize under hypoxia and other stress conditions. The resulting RBC sickling, vaso-occlusion, and attendant tissue ischemia, it was recognized, contributed to the harrowing crisis episodes experienced recurrently by patients with SCD.1-4

28. **Simple visual reaction time in sickle cell disease patients of pediatric age group**

    2017

    National Journal of Physiology, Pharmacy and Pharmacology

    Jagzape, Arunita and Jagzape, Tushar and Deshpande, Vijay

Sickle Cell Disease; Simple Visual Reaction Time; Cohen's d INTRODUCTION Reaction time (RT) can be defined as time interval between presentation of stimulus and appearance of appropriate voluntary response in a person, usually expressed in milliseconds.11"31 Speed of flow of neurophysiological, cognitive, and information process created by the action of stimulus on the sensory system is reflected through RT. In view of this research gap analysis, this study was planned with the objective to record changes in VRT in sickle cell patients of pediatric age group as compared to controls. Ophthalmic examination was performed by ophthalmologists after the VRT, and the protocol was that if the participant had refractive error or obvious signs of retinal and optic nerve involvement, the data of those participants were excluded. DISCUSSION VRT is the time taken to react to a visual stimulus by an individual and acts as a reliable indicator of processing rate of sensory stimuli by central nervous system and its motor response leading to the execution of a task.

29. **Distal renal tubular acidosis in sickle cell anemia**

    2018

    Saudi Journal of Kidney Diseases and Transplantation

    Bharani, Anjali and Manchanda, Rani and Singh, Ritesh and Prashant, Swati

We report a rare case of two young male siblings with sickle cell anemia who presented with bilateral lower limb deformities, failure to thrive, polyuria, and polydipsia. On investigations, they were found to have normal anion gap metabolic acidosis, hypokalemia, and nephrocalcinosis were seen on ultrasonography of the kidneys. These reports were suggestive of distal renal tubular acidosis (dRTA). They were started on oral alkali replacement and potassium therapy with which clinical improvement was seen. Conventionally, renal tubular dysfunction is thought to occur infrequently in patients with sickle cell anemia. Hence, we report this rare association between sickle cell anemia and dRTA.

30. **Assessment of Periodontal Health in Patients with Sickle Cell Disease (SCD)**

    2018

    Journal of Advanced Medical and Dental Sciences Research

Background: Sickle cell disease (SCD) is an inherited disease in individuals homozygous for hemoglobin S. Numerous oral manifestations of SCD that affect the oral mucosa, gingival tissue, mandible, nerve supply, and

tooth enamel and pulp have been reported. Aim of the study: To assess the periodontal health in patients with sickle cell disease. Materials and methods: The study was conducted in the Department of Periodontics of the dental institution. A total of 30 patients with SCD from the medical hospital were included in the study group. Study group comprised of sickle cell disease patients of both sex and varying age groups. A control group of 20 patients matched for age and sex was also included. Study was conducted for a period of one year. Results: The number of male patients was 14 and he number of female patients was 16.The mean plaque index in sickle cell disease group was 3.11Â±1.16 and in control group was 2.1Â±0.89. The mean gingival index of sickle cell disease group was 2.75Â±1.77 and in control group was 1.82 Â± 0.87. Conclusion: The periodontal diseases are very prevalent in patients with sickle cell disease. Thus, preventive dental care is very important for SCD patients.

31. **C-Window Peaks on CE-HPLC are Extremely Rare in Northern India, and Only Infrequently Represent HbC**

    2018

    Indian Journal of Hematology and Blood Transfusion

    Dass, Jasmita and Mittal, Suchi and Saraf, Amrita and Kotwal, Jyoti

Hemoglobin C (HbC, HBB:c.19GÂ >Â A) is a structural variant that has been reported rarely from India. This was a retrospective review of all high performance liquid chromatography (HPLCs) submitted over a 14Â year period to a tertiary care center in North India with an aim of finding hemoglobins that elute in the C-window. Of the 32,364 HPLCs screened, 6 cases showed peaks in the C-window. Of these 6 cases, only two cases contained hemoglobin C. These was one case each of HbC/Î² thalassemia and compound heterozygosity for HbC and HbD. There were 4 cases which showed very similar red cell indices and chromatograms with multiple peaks eluting in D-window, C-window and an additional peak with a retention time of 4.74Â min. These four cases were compound heterozygous for an Î± chain variant HbQ-India and a Î²-chain variant HbD.

32. **Multiple Vertebral Necrosis in a Sickle Cell Trait: A Rare Manifestations**

    2014

    Indian Journal of Hematology and Blood Transfusion

    Taksande, Bharati Amar and Kotpalliwar, Sujay and Sabarwal, Shagun and Patil, M

Sickle cell trait also called sicklemia is a condition in which a person has one abnormal allele of the hemoglobin beta gene and is heterozygous, but does not display the severe symptoms of sickle cell disease that occur in a person who has two copies of that allele. Sickle cell trait is a hemoglobin genotype AS is generally regarded as a benign condition. We present a rarest case of young female of sickle cell trait having multiple vertebrae necrosis.

33. **Erythrocyte microRNAs: a tiny magic bullet with great potential for sickle cell disease therapy**
    2021

    Annals of Hematology

    Verma, Henu Kumar and Ratre, Yashwant Kumar and Bhaskar, L V K S and Raffaella, Colombatti

Sickle cell disease (SCD) is a severe hereditary blood disorder caused by a mutation of the beta-globin gene, which results in a substantial reduction in life expectancy. Many studies are focused on various novel therapeutic strategies that include re-activation of the Î³-globin gene. Among them, expression therapy caused by the fetal hemoglobin (HbF) at a later age is highly successful. The induction of HbF is one of the dominant genetic modulators of the hematological and clinical characteristics of SCD. In fact, HbF compensates for the abnormal beta chain and has an ameliorant effect on clinical complications. Erythropoiesis is a multi-step process that involves the proliferation and differentiation of a small population of hematopoietic stem cells and is affected by several factors, including signaling pathways, transcription factors, and small non-coding RNAs (miRNAs).

miRNAs play a regulatory role through complex networks that control several epigenetic mechanisms as well as the post-transcriptional regulation of multiple genes. In this review, we briefly describe the current understanding of interactions between miRNAs, their molecular targets, and their regulatory effects in HbF induction in SCD.

34. Acute cortical necrosis following renal transplantation in a case of sickle cell trait

2011

Indian Journal of Nephrology

***Shiradhonkar, S and Jha, R and Rao, B and Narayan, G and Sinha, S and Swarnalata,* G**

Renal transplant recipients who have sickle cell disease are at risk of infection, recurrent graft disease, and sickling crisis that affects the long-term outcome. We report a patient of sickle cell trait who developed patchy cortical necrosis in the perioperative period but had a good long-term outcome. The renal cortical necrosis was presumed to be secondary to cyclosporine-basiliximab interaction in the backdrop of sickling trait. The patient additionally had spontaneous closure of vascular access and severe hypertension immediately following transplantation suggestive of vaso-occlusive crisis. Cyclosporine and basiliximab drug interaction needs to be recognized and steps need to be taken in patients to avoid perioperative graft dysfunction.

35. Acute splenic infarction in a hiker with previously unrecognised sickle cell trait

2013

BMJ Case Reports

Gupta, Monica and Lehl, S S and Singh, Kamal and Singh, Ram

Description Acute splenic infarction in otherwise asymptomatic individuals harbouring sickle cell trait (SCT) may occur when they are exposed to low oxygen tension at high altitudes. 1 The first ever case report of splenic infarction in SCT was published way back in 1954 by Cooley et al. 2 Since then many similar cases have been reported worldwide and discussed at length. 3 The case we are highlighting here is that of a young healthy 21-year-old man, born in Punjab, India who went mountain climbing (for the first time) at Nanda devi, Garhwal Himalayas (Uttarakhand), with an altitude of 5025 m above sea level.

36. Comorbidities in sickle cell disease: Adult providers needed!

2018

The Indian Journal of Medical Research

Ogu, Ugochi and Billett, Henny

SCD was first reported in the western literature in 1910 by Dr. James Herrick, however, it took almost 40 more years until, in 1949, Linus Pauling demonstrated that the disease originated from a mutated haemoglobin (Hb) and then another 18 years when, in 1957, Vernon Ingram discovered that a single amino acid substitution (glutamic acid to valine), due to a change in a single nucleotide (adenine to thymidine), was responsible for the disease[1],[2]g. Under deoxygenated conditions, this mutated HbS undergoes polymerization, leading to intracellular tactoid formation and deformation of the red blood cells to an irreversibly sickled state. Chronic comorbidities such as avascular necrosis (AVN), leg ulcers, pulmonary hypertension (PH), diastolic heart dysfunction, gout, end-stage renal disease (ESRD) and ophthalmologic complications increase with age. The ulcer may limit the mobility of adult patients, who also develop a phobia of being around people or attending social events, especially if they have large ulcers and/or the ulcers have an emanating odour. Because of the stigma, they encounter from having a leg ulcer; these patients may limit their social interaction. [...]the comorbidities in SCD are myriad and substantial and will only increase as the average lifespan increases.

37. Clinical profile of sickling disorders with reference to genotype-phenotype association

1982

Indian Pediatrics

Rath, B K and Parija, A C and Sen, S K

100 sickling positive cases were subjected to detailed clinical examination. Hemoglobin genotypes were established by Agar-gel electrophoresis (pH 6.2), family study and fetal hemoglobin estimation. The clinical features were correlated with the individual genotypes. The study revealed that sickle cell anemia (SS) is frequently associated with different crises. Aplastic and sequestration crises are exclusively seen in 'SS' states. Sickle-thalassemia (S-thal), however, is a less severe from having moderate anemia. But in contrast to 'SS' state, splenomegaly is a uniform finding in these cases. Sickle cell trait patients are mostly normal individuals with mild anemia and usually do not suffer from crises. However, painless hematuria is frequently observed in these cases.

38. Cation exchange high performance liquid chromatography for diagnosis of haemoglobinopathies

2009

Medical Journal Armed Forces India

Gupta, P K and Kumar, H and Kumar, S and Jaiprakash, M

Background: Cation exchange high performance liquid chromatography (HPLC) is emerging as the method of choice for initial screening and diagnosis of haemoglobinopathies. The use of alkaline and acid gel electrophoresis in the developing countries may result in incorrect diagnosis of haemoglobinopathies. The aim of the study is to assess the accuracy and precision of diagnosis of haemoglobinopathies by HPLC and its possible advantage over conventional techniques. Methods: Over a two year period, 955 patients presenting with anaemia were evaluated by HPLC for diagnosis of haemoglobinopathies. All cases showing 'unknown peaks' and other rare haemoglobin variants on HPLC were further analyzed by agar gel electrophoresis at alkaline pH (8.6) and at acid pH (6.0). Result: A total of 137 (14.3%) patients showed different abnormal haemoglobins variants. Of these 91 (66.4%) were diagnosed to have beta - heterozygous thalassaemia based on high level of HbA2 (>3.9%), five (3.7%) as beta - homozygous thalassaemia (HbF 25 - 91%), 15 (10.9%) as sickle cell trait, two (1.5%) as compound heterozygous state of sickle - Î²+ thalassaemia and three (2.2%) patients as homozygous sickle cell anaemia (HbSS). One (0.7%) patient had unknown peak on HPLC with retention time of 4.78 minutes, constituting 16.8% of total haemoglobin. Sickling test was negative. He was diagnosed as HbQ - India heterozygous. Thirteen (9.5%) patients were diagnosed as HbE syndrome and were further sub classified as HbE trait (five cases) and HbE disease (eight cases). Seven (5.1%) patients were diagnosed as Hb - D Punjab heterozygous. Conclusion: The simplicity of the sample preparation, superior resolution of the method and accurate quantitation of haemoglobin concentration, combined with complete automation, makes this an ideal methodology for diagnosis of haemoglobinopathies.

39. Genotypic influence of Î±-deletions on the phenotype of Indian sickle cell anemia patients.

2011

The Korean journal of hematology

Pandey, Sanjay and Pandey, Sweta and Mishra, Rahasya Mani and Sharma, Monica and Saxena, Renu

BACKGROUND: Some reports have shown that co-inheritance of Î±-thalassemia and sickle cell disease improves hematological parameters and results in a relatively mild clinical picture for patients; however, the exact molecular basis and clinical significance of the interaction between Î±-thalassemia and sickle cell disease in India

has not yet been described. There is little agreement on the clinical effects of Î±-thalassemia on the phenotype of sickle cell disease. METHODS: Complete blood count and red cell indices were measured by an automated cell analyzer. Quantitative assessment of hemoglobin variants HbF, HbA, HbA(2), and HbS was performed by high performance liquid chromatography (HPLC). DNA extraction was performed using the phenol-chloroform method, and molecular study for common Î±-deletions was done by gap-PCR. RESULTS: Out of 60 sickle cell anemia patients, the Î±-thalassemia genotype was found in 18 patients. Three patients had the triplicated Î±-genotype (Anti Î±-3.7 kb), and the remaining patients did not have Î±-deletions. This study indicates that patients with co-existing Î±-thalassemia and sickle cell disease had a mild phenotype, significantly improved hematological parameters, and fewer blood transfusions than the patients with sickle cell anemia without co-existing Î±-deletions. CONCLUSION: Co-existence of Î±-thalassemia and sickle cell anemia has significant effects on the phenotype of Indian sickle cell patients.

40. Coevality of Systemic Lupus Erythematosus With Sickle Cell Trait: A Not So Uncommon Entity.

2020

Cureus

Das, Dhriti Sundar and Sahoo, Debananda

The coexistence of systemic lupus erythematosus (SLE) with sickle cell trait is quite sparingly reported in literature. Here, we narrate the case of a 17-year-old girl from Eastern India with sickle cell trait who presented with acute lupus pneumonitis. The challenges to the final diagnosis of SLE with sickle cell trait were because of the often lesser degree of clinical suspicion at the outset. In this report, we discuss this not so uncommon combination of conditions and review related literature. This girl, who was a known case of sickle cell trait, presented with fever, cough, shortness of breath with subsequent rashes, oral ulceration, highÂ erythrocyte sedimentation rate (ESR)Â and proteinuria. After ruling out infective causes, sheÂ was found to be antinuclear antibody (ANA) positive and with stage 4 lupus nephritis. Emphasis should be given to the presence of autoimmune conditions in patients with sickle hemoglobinopathies, including sickle cell trait wherein atypical or systemic involvement may occur. Such association holds more importance as sickle hemoglobinopathies is one of the major hemoglobinopathies reported in this part of the country.

41. Population and Public Health Implications of Child Health and Reproductive Outcomes Among Carrier Couples of Sickle Cell Disorders in Madhya Pradesh, Central India.

2014

International journal of MCH and AIDS

Balgir, Ranbir S

BACKGROUND: Sickle cell disease is a major genetic and public health challenge in India. Adequate studies on clinico-hematological aspects of disorders are available, however there are few studies on the public health and reproductive outcomes among sickle cell carrier couples. METHODS: A total of 383 couples including their offspring with at least one case of sickle cell disorder referred to a testing center from a tertiary hospital from March 2010 to February 2013 were consecutively studied as matched case controls. RESULTS: Out of 383 couples, 200 were found normal and 183 had different sickle cell disorders. Carrier couples of sickle cell disease had significantly higher fertility (mean number of conceptions, i.e. 3.153 versus 1.480) and higher below 10 year mortality (11% versus 2.7%) and lower surviving offspring (877.4 versus 970.6) than of controls. Neonatal and infant mortality was doubled (34.3 versus 14.7) and three-fold higher (44.1 versus 14.7), respectively in carriers of disease per 1000 live-births compared to controls. Couples of AS/SS genotype showed high neonatal, infant, below 10 year mortality (214.3 each) and low surviving offspring (785.7 per 1000 live-births). CONCLUSIONS AND GLOBAL HEALTH IMPLICATIONS: Sickle cell carrier couples are increasing in both trait and disease offspring (surviving: 56.7% against 43.3% normals). This increased production of carrier and disease offspring leads to increased morbidity, neonatal/infant and childhood mortality, and adversely affects the survival fitness.

42. HbSD-Punjab: Clinical and hematological profile of a rare hemoglobinopathy

2014

Journal of Pediatric Hematology/Oncology

Oberoi, S and Das, R and Trehan, A and Ahluwalia, J and Bansal, D and Malhotra, P and Marwaha, R K

PURPOSE: Compound heterozygous HbSD-Punjab is an uncommon hemoglobinopathy encountered in Indians. Limited literature is available about its clinical course. The aim of this study was to describe the clinical and hematological profile of HbSD-Punjab patients from North India. MATERIALS AND METHODS: HbSD-Punjab patients diagnosed in the hematology clinics between year 2000 and 2010 were reviewed retrospectively. The diagnosis was established using high-performance liquid chromatography, molecular analysis, and family screening. Clinical details, laboratory parameters, and therapy details were recorded from case records. RESULTS: Ten patients were identified. Median age at onset of symptoms was 3.5 years (interquartile range [IQR], 1.9 to 7.2). Clinical presentation included: anemia in 3, painful vaso-occlusive crisis in 2, acute chest syndrome in 2, and 3 were diagnosed incidentally. All had moderate to severe anemia (mean hemoglobin [Hb]: 6.8Â±1.2 g/dL). Eight required red cell transfusions (median: 3 [IQR, 2 to 8]). On high-performance liquid chromatography, median HbF, HbD, and HbS were 12.1% (IQR, 9 to 18.3), 39.7% (IQR, 35 to 42), and 38.5% (IQR, 29 to 43). Five patients received hydroxyurea (HDU), median dose: 20 mg/kg/d (IQR, 18 to 23) with median duration of 7 months (IQR; 6, 45). Increment in Hb and reduction in painful crisis was observed in response to HDU. CONCLUSIONS: HbSD-Punjab has a heterogeneous clinical presentation. Anemia and sickle crises are quite common. HDU may be considered for those presenting with severe phenotype. Â© 2014 by Lippincott Williams & Wilkins.

43. Attrition from care and clinical outcomes in a cohort of sickle cell disease patients in a tribal area of western India

2019

Tropical Medicine and Infectious Disease

Dave, K and Chinnakali, P and Thekkur, P and Desai, S and Vora, C and Desai, G

In a tribal area of western India, a non-governmental organization implemented a comprehensive sickle cell disease (SCD) program at a secondary level hospital. In a cohort of SCD patients registered during December 2015 to June 2017, we assessed rates of lost to follow-up (LTFU) during the follow-up period using routinely collected data. We compared the uptake of proven interventions and indicators of disease severity from one year prior to registration until the end of the study (June 2018). Of 404 patients, the total follow-up duration was 534 person-years (PY). The rate (95% CI) of LTFU was 21 (17.5â€“25.3) per 100 PY. The proportion of people who received the pneumococcal vaccine improved from 10% to 93%, and coverage of hydroxyurea improved from 3.5% to 88%. There was a statistically significant decrease in rates (per 100 PY) of pain crisis (277 vs 53.4), hospitalization (49.8 vs 42.2), and blood transfusion (27.4 vs 17.8) after enrollment in the SCD program. Although clinical intervention uptake was high, one quarter of the patients were LTFU. The study demonstrated significant reductions in disease severity in SCD patients.

44. Spectrum of hemoglobinopathies in the state of Orissa, India: A ten years cohort study

2005

Journal of Association of Physicians of India

Balgir, R S

Objectives: i) To determine the pattern of spectrum of hemoglobinopathies in the state of Orissa, ii) To find the ethnic groups at high risk of hemoglobinopathies, iii) Geographical distribution of hemoglobinopathies, and iv). To know epidemiological aspects of hemoglobinopathy cases in Orissa. Material and Methods: One thousand fifteen cases of anemia were analysed referred from different peripheral hospitals and Medical Colleges and

Hospitals of Orissa state for diagnosis and counseling during 1994 to 2003. About 2-3 ml. intravenous blood samples were collected after obtaining informed consent from each individual. Hematological indices were measured using MS4 Cell Counter. Background data of each individual were recorded like age, sex, caste, place of origin, consanguinity, etc. Hemoglobin electrophoresis was carried out on CAM in Tris-EDTA-Borate buffer at pH 8.9 and quantification of A2 fraction of hemoglobin by elution method. The value more than 3.5% of A2 fraction of hemoglobin was taken as cut off point for Î².thalassemia trait and more than 10% as Hb E. Hb electrophoresis in acidic medium (pH 6.2) was also carried out to confirm Hb D or E band. Estimation of fetal hemoglobin was done. Family studies were carried out to confirm the diagnosis. Results: Most common hemoglobinopathies observed out of 1015 cases were: sickle cell trait (29.8%), sickle cell disease (7.5%), sickle cell-Î²-thalassemia (1.7%), Î²-thalassemia trait (18.2%), thalassemia major (5.3%), thalassemia intermedia (0.9%), Hb E trait (0.9%), Hb E disease (0.3%), E-Î²-thalassemia (0.7%), Hb D trait (0.2%) and SD disease (0.2%). Sickle cell disorders with high level of fetal hemoglobin were common in general castes (0.3-20.7%), scheduled castes (0-8.9%) and scheduled tribals (0-5.5%). Transfusion dependent Î²-thalassemia syndrome was prevalent in Brahmin, Karan, Khandyat, Teli, etc. Most of the cases belong to Anugul district, followed by Khurda, Nayagarh, Phulbani, Cuttack, Jajpur, Dhenkanal, Ganjam, Keonjhar, Mayurbhanj, etc. Conclusions: The heterogeneous population is harbouring almost all major hemoglobinopathies in general castes, scheduled castes and tribes, belonging to Coastal and South-Western regions of Orissa. This study provides for the first time a comprehensive database on the pattern of spectrum of hemoglobinopathies in Orissa. Â© JAPI.

45. Homozygous sickle cell disease in Central India & Jamaica: A comparison of newborn cohorts

2020

Indian Journal of Medical Research, Supplement

Jain, D and Tokalwar, R and Upadhye, D and Colah, R and Serjeant, G R

Background & objectives: Homozygous sickle cell (SS) disease in Central India runs a more severe clinical course than reports from other areas of India. The current study was undertaken to compare the disease in Central India (Nagpur) with that in Jamaica, both populations defined by newborn screening. Methods: The Nagpur cohort included infants born to sickling-positive mothers from May 2008 to 2012, examined by high-pressure liquid chromatography and DNA analysis. The Jamaican cohort screened 100,000 consecutive non-operative deliveries between June 1973 and December 1981, analyzed by haemoglobin (Hb) electrophoresis and confirmed by family studies and compatible HbA2 levels. Results: In Nagpur, 103 SS patients were detected, but only 78 (76%) were followed up. In Jamaica, 311 cases were followed from birth and compliance with follow up remained 100 per cent up to 45 years. In the Nagpur cohort all had the Asian haplotype, and 82 per cent of Jamaicans had at least one Benin chromosome; none had the Asian haplotype. Compared to Jamaica, Nagpur patients had higher foetal Hb, less alpha-thalassaemia, later development of splenomegaly and less dactylitis. There were also high admission rates for febrile illness and marked anaemia. Invasive pneumococcal disease occurred in 10 per cent of Jamaicans but was not seen in Nagpur. Interpretation & conclusions: There were many differences between the disease in Nagpur, Central India and the African form observed in Jamaica. The causes of severe anaemia in Nagpur require further study, and reticulocyte counts may be recommended as a routine parameter in the management of SS disease. The role of pneumococcal prophylaxis needs to be determined in Nagpur patients. Future studies in India must avoid high default rates.

46. Fetal haemoglobin and Î²-globin gene cluster haplotypes among sickle cell patients in Chhattisgarh

2013

Journal of Clinical and Diagnostic Research

Bhagat, S and Patra, P K and Thakur, A S

Background: Foetal Haemoglobin (HbF) is the best-known genetic modulator of sickle cell anaemia, which varies dramatically in concentration in the blood of these patients. The patients with SCA display a remarkable variability in the disease severity. High HbF levels and the Î²-globin gene cluster haplotypes influence the clinical presentation of sickle cell disease. To identify the genetic modifiers which influence the disease severity, we conducted a Î²-globin haplotype analysis in the sickle cell disease patients of Chhattisgarh. Aim: The foetal haemoglobin and the Î²-globin gene haplotypes of the sickle cell trait and the sickle cell disease patients from Chhattisgarh were investigated. Materials and Method: A total of 100 sickle cell patients (SS), 50 sickle cell trait patients (AS) and 50 healthy control individuals were included in the present study. The distribution of the Î²-globin gene haplotype was done by the PCR-RFLP method. Result: PCR-RFLP showed that the homozygous Arab-Indian haplotype (65%) was the most frequent one, followed by the heterozygous Arab-Indian haplotype (11%) in the sickle cell patients (SS), while the AS patients had a higher frequency of the heterozygous Arab-Indian haplotype (38%) in comparison to homozygous one (32%). Four atypical haplotypes, 3 Benin and 1 Cameroon were also observed, although they were in lower frequencies. In the present study, the HbF levels were higher in the AS and the SS patients, with one or two Arab-Indian haplotypes as compared to the other haplotypes. Conclusion: The presence of the Arab-Indian haplotype as the predominant haplotype might be suggestive of a gene flow to/ from Saudi-Arabia or India and it was associated with higher HbF levels and a milder disease severity.

47. Improving the Capacity of Health System and Community for Sickle Cell Disease Screening and Management Among Tribal Population in India: Protocol of an Intervention Study.

2020

Current health sciences journal

Babu, Bontha V and Sridevi, Parikipandla and Surti, Shaily B and Ranjit, Manoranjan and Bhat, Deepa and Sarmah, Jatin and Sudhakar, Godi and Sharma, Yogita

Sickle cell disease (SCD) is one of the major public health problems in the world. In India, the burden of SCD is comparatively high in socio-economically disadvantaged tribal communities. Though efficacious interventions are available to manage SCD, they are not reaching to these communities and no comprehensive programme is in place in the health care system. Therefore, the Indian Council of Medical Research has initiated a nation-wide study to develop an effective intervention model for SCD patients in tribal areas through the government health care system. This intervention includes increasing awareness and preparing the communities for accessing the government health care system for SCD care, and improving the capacity of the primary health care systems including the training of the health care providers on prevention and management of SCD. The study adopted a quasi-experimental design with pre-vs. post-intervention comparisons of outcome variables within the interventional groups and with the control group. The study will be implemented in 6 districts which are endemic for SCD, spread across different geographical zones of India. In each district, four primary health centre (PHC) areas which are predominantly inhabited by tribal population will be selected. Of these four PHC areas, two will be selected randomly for implementing the intervention and the remaining two will be the control area. Information necessary for development and implementation of the intervention will be gathered during formative research, by using both quantitative and qualitative research methods. Intervention with an inclusive partnership and community mobilization will be implemented. The major steps in the implementation of intervention are partnership building with various health and non-health partners including the community. Capacity building and strengthening is another important component to enable the primary health facilities to screen and manage SCD patients. Primarily, sub-health centres and primary healthcare centres will be equipped with appropriate SCD screening techniques. All doctors in the system will be trained in advanced treatment and management issues. To improve the community's awareness and readiness, community mobilization activities will be conducted. An impact evaluation will be carried out at the end of the intervention by comparing the improvement of SCD management in intervention PHCs to that of the control PHCs. However, the process evaluation and necessary mid-term corrections will be made throughout the intervention period. Thus, an intervention model in terms of its suitability, replicability and sustainability for the tribal population will be developed and tested. The findings of this study are more suitable to use during advocacy and to replicate the model by the state health departments.

This study develops and places an appropriate referral system for SCD patients at the PHC level. Improving the community's access to health care, improving the quality of care in government health centres and raising awareness among tribal communities are crucial to achieving through innovation. Taken together, these innovations would significantly contribute to better access to health care and management of the SCD patients of underserved tribal population.

48. Dental and periodontal health status of Beta thalassemia major and sickle cell anemic patients: a comparative study.

2013

Journal of international oral health : JIOH

Singh, Jaideep and Singh, Nitin and Kumar, Amit and Kedia, Neal Bharat and Agarwal, Anil

BACKGROUND: This study aimed to assess the dental and periodontal health status of beta thalassemia major and sickle cell anemic patients in Bilaspur, Chattishgarh, India. MATERIALS & METHODS: A total of 750 patients were included in the study. The patients were randomly divided into three groups I (n=250), II (n=250) and III (n=250), ranging from 3-15 years. After performing a thourough general examination, including their demographic data, intraoral examination was done using Decayed-Missing-Filled Teeth Index (DMFT Index), Plaque index (PI) and Gingival index (GI). Statistical analysis was done using statistical software SPSS 17.5 version. Chi square test & student t test was used for the comparison of study and control groups. The level of significance was set at P<0.05. RESULTS: In the present study, it was found that, prevalence of dental caries and periodontal diseases was significantly more in beta thalassemic patients followed by sickle cell anemic patients than control group. However, when group I (beta thalassemia) was compared with group II (sickle cell anemia), results were found to highly significant (P<0.001) only for decayed missing filled tooth. CONCLUSION: Appropriate dental and periodontal care improves a patient's quality of life. Preventive dental care is must for thalassemic and Sickle cell disease patients. How to cite this article: Singh J, Singh N, Kumar A, Kedia NB, Agarwal A. Dental and Periodontal Health Status of Beta Thalassemia Major and Sickle Cell Anemic Patients: A Comparative Study. J Int Oral Health 2013; 5(5):53-8.

49. Clinical and hematological presentation among Indian patients with common hemoglobin variants

2014

Clinica Chimica Acta

Italia, K and Upadhye, D and Dabke, P and Kangane, H and Colaco, S and Sawant, P and Nadkarni, A and Gorakshakar, A and Jain, D and Italia, Y and Ghosh, K and Colah, R

Background: Co-inheritance of structural hemoglobin variants like HbS, HbDPunjab and HbE can lead to a variable clinical presentation and only few cases have been described so far in the Indian population. Methods: We present the varied clinical and hematological presentation of 22 cases (HbSDPunjab disease-15, HbSE disease-4, HbDPunjabE disease-3) referred to us for diagnosis. Results: Two of the 15 HbSDPunjab disease patients had moderate crisis, one presented with mild hemolytic anemia; however, the other 12 patients had a severe clinical presentation with frequent blood transfusion requirements, vaso occlusive crisis, avascular necrosis of the femur and febrile illness. The 4 HbSE disease patients had a mild to moderate presentation. Two of the 3 HbDPunjabE patients were asymptomatic with one patient's sibling having a mild presentation. The hemoglobin levels of the HbSDPunjab disease patients ranged from 2.3 to 8.5g/dl and MCV from 76.3 to 111.6fl. The hemoglobin levels of the HbDPunjabE and HbSE patients ranged from 10.8 to 11.9 and 9.8 to 10.0g/dl whereas MCV ranged from 67.1 to 78.2 and 74.5 to 76.0fl respectively. Conclusions: HbSDPunjab disease patients should be identified during newborn screening programmes and managed in a way similar to sickle cell disease. Couple

at risk of having HbSDPunjab disease children may be given the option of prenatal diagnosis in subsequent pregnancies. Â© 2014 Elsevier B.V.

50. Cognitive functions and psychological problems in children with Sickle cell anemia

2016

Indian Pediatrics

Rajendran, G and Krishnakumar, P and Feroze, M and Gireeshan, V K

Objective: To study the cognitive functions and psychological problems in children with Sickle cell anemia (SCA). Methods: Children with SCA were compared with an age-, sex- and community- matched control group of children with no SCA. Malinâ€™s Intelligence Scale for Indian children, modified PGI memory scale, and Childhood Psychopathology Measurement Schedule were used to assess cognitive functions and psychological problems. Results: Verbal quotient, performance quotient and intelligence quotient in SCA group were 77, 81, 78, respectively versus 92, 95, 93, respectively in non-SCA group (P <0.001). Borderline intellectual functioning and mild mental retardation were more common in SCA (70% and 16%, respectively). Children with SCA had impaired attention, concentration and working memory and more behavior problems compared to children without SCA. Conclusions: Cognitive functions are impaired in children with SCA and they have more psychological problems. Facilities for early identification and remediation of psychological and intellectual problems should be incorporated with health care services for children with sickle cell anemia.

51. Pregnancy outcomes in women with sickle cell disease: a retrospective study from Eastern India.

2019

Journal of Obstetrics & Gynaecology

Patel, Siris and Purohit, Prasanta and Jit, Bimal Prasad and Meher, Satyabrata

Sickle cell disease is a major public health problem in the state of Odisha, India, with significant morbidity and mortality. It is characterised by chronic haemolytic anaemia and repeated episodes of vaso-occlusive crises, which lead to an increased morbidity and mortality, besides multi-organ failure. Pregnancy with sickle cell disease is considered high risk. Women experience many complicationsâ€”both sickle cell disease related and obstetric (maternal as well as foetal).

52. Clinical events in a large prospective cohort of children with sickle cell disease in Nagpur, India: evidence against a milder clinical phenotype in India.

2016

Pediatric Blood & Cancer

Jain, Dipty and Arjunan, Aishwarya and Sarathi, Vijaya and Jain, Harshwardhan and Bhandarwar, Amol and Vuga, Marike and Krishnamurti, Lakshmanan

Background: The clinical phenotype of sickle cell disease (SCD) has been reported to be milder in India than in the United States. The objective of this large single-center study was to examine the rate of complications to define the phenotype of SCD in India.Methods: The rate of complications per 100 person-years in 833 pediatric SCD patients for 1954 person-years in Nagpur, India including those diagnosed on newborn screen (NBS) and those presenting later in childhood (non-NBS) was compared to those reported in the cooperative study of sickle cell disease (CSSCD). Event rates were also compared between patients belonging to scheduled castes (SCs), scheduled tribes (STs), and other backward classes (OBC).Results: Comparison of CSSCD versus Nagpur NBS versus Nagpur non-NBS for rates of pain (32.4 vs. 85.2 vs. 62.4), severe anemia (7.1 vs. 27 vs. 6.6), stroke (0.7 vs. 0.8 vs. 1.4), splenic sequestration (3.4 vs. 6.7 vs. 1.6), acute chest syndrome (24.5 vs. 23.6 vs. 1.0), and meningitis (0.8 vs. 0 vs. 0.1) revealed more frequent complications in Nagpur compared to CSSCD. Comparison

of ST, SC, and OBC for rates of pain (84.6 vs. 71.9 vs. 63.5), acute chest syndrome (3.6 vs. 2.8 vs. 2.2), severe anemia (5.4 vs. 9.5 vs. 11.4), stroke (1.2 vs. 0.4 vs. 0.3), splenic sequestration (0.6 vs. 2.4 vs. 1.9), and meningitis (0.8 vs. 0 vs. 0.1) revealed significantly more frequent complications among ST.Conclusions: SCD-related complications are more frequent in Indian children than that observed in CSSCD. Further study is indicated to define SCD phenotype in India.

53. Sickle cell disease presenting in the third trimester of pregnancy: Delayed detection heralding a public health problem?

2020

Indian Journal of Public Health

Sharma, Ankita and Gaur, Kavita and Tiwari, Vandana and Shukla, Shailaja and Tiwari, Vandana Puri

We report the case of a 22-year-old primigravida detected as having sickle cell disease (SCD), initially presenting in the third trimester (30th week) of pregnancy. The patient came to our center with a complaint of severe lower limb pain. The peripheral smear showed marked anisopoikilocytosis, numerous leptocytes, sickle cells, and target cells. High-performance liquid chromatography corroborated the diagnosis of SCD, showing a significant peak in the sickle window. The patient was conservatively managed and delivered a healthy baby through normal vaginal delivery. Delayed presentation of SCD in the third trimester of pregnancy is unusual. This report aims to bring attention to the possible causes of such a lag in detection. We also suggest measures to refine the antenatal healthcare screening at multiple levels, with regard to the detection of sickle cell hemoglobinopathy.

54. Inherited blood disorders, genetic risk and global public health: framing â€˜birth defectsâ€™ as preventable in India.

2018

Anthropology & Medicine

Chattoo, Sangeeta

This paper engages critically with the global assemblage framing sickle cell and thalassaemia disorders as a â€˜global health crisisâ€™; and the promise of genomics, largely DNA-based carrier/pre-conceptual screening, prenatal diagnosis with a view to terminations, deployed in framing a solution to these historically racialised spectrum of diseases as essentially preventable. Sickle cell and thalassaemia are recessively inherited, potentially life-threatening haemoglobin disorders with significant variation of severity, often needing life-long treatment. I argue that the re-classification of inherited blood disorders (IBDs) under â€˜prevention and management of birth defectsâ€™ by the WHO in 2010 can be read as an ethical moment within the â€˜globalising turnâ€™ of IBDs and the use of genomics in addressing structural inequalities underpinning health in low- and middle-income countries. Using an Indian case study, the paper aims at first examining the language of risk through which genes and IBDs are mapped onto pre-existing populations (e.g. caste and tribe) as discrete, categories. Second, it discusses the likely social and ethical ramifications of classifying these recessive gene disorders as essentially preventable, despite cheaply available diagnostic tests and treatment options available in most countries in the South.

55. Association of a high oxygen affinity hemoglobin Abruzzo with HbS: first family study from Central India.

2016

International Journal of Laboratory Hematology

Shrikhande, A V and Pawar, P S

The article presents a case study of a 30-year-old Indian woman who was asymptomatic. Topics discussed include performance of hemoglobin electrophoresis by capillary electrophoresis; high-performance liquid chromatography (HPLC); and husband diagnosed with relative polycythemia with erythrocytosis. Other topics include a table presenting hematological data of mother, father and child; and disorders related to high oxygen affinity hemoglobin Abruzzo with Sickle hemoglobin (HbS).

56. Red blood cell exchange in sickle cell disease patient with multiple alloantibodies.

2020

Asian Journal of Transfusion Science

Aggarwal, Geet and Tiwari, Aseem and Dhiman, Pratibha and Arora, Dinesh and Pabbi, Swati and Setya, Divya

There are several reports in medical literature about Red Cell Exchange (RCE) being routinely performed pre-operatively in sickle cell disease patients to provide immediate decrease in HbS concentration and prevent post-operative complications. We would like to present one such case of SCD who also had multiple allo-antibodies and had to undergo hemi-arthroplasty for avascular necrosis of head femur. Grouping and antibody screening was performed using column agglutination technique. 3-cell and 11- cell panel were used for antibody screening and identification, respectively. Automated RBC exchange was performed on apheresis machine Com.Tec using the standard PL1 kit (Fresenius Kabi, Germany). Multiple (anti-c, E) allo-antibodies were identified and successful pre-operative RCE was done with corresponding antigen-negative AHG compatible RBC units. Single RCE procedure reduced HbS concentration from 65% to 25%. The patient underwent uneventful hemi-arthroplasty and was discharged on post-operative day-7. Patient is on regular follow-up and continues to do well two months after the day of surgery. This is possibly the first case report from India, which illustrates successful automated RCE in a SCD patient with alloimmunization.

57. Pulmonary Function Tests in Sickle Cell Disease.

2016

Indian Journal of Pediatrics

Purohit, Raviraj and Rao, Sanjeev and Goyal, Jagdish and Shah, Vijay and Charan, Jaykaran and Rao, Sanjeev S and Goyal, Jagdish P and Shah, Vijay B

Objective: To determine pulmonary function abnormalities in children with Sickle Cell Disease (SCD) from Western India.Methods: In this cross sectional study conducted at Surat, Gujarat, India; equal number of age and gender matched children i.e., 99 in the age group of 6-18Â y was recruited in case (children with SCD) and control (non-SCD healthy children) groups respectively. Weight, height, body mass index (BMI) and hemoglobin (Hb) were assessed as baseline characteristics and spirometry was performed to assess the pulmonary function.Results: The two groups of children were comparable in the baseline characteristics such as weight, height and BMI, however mean hemoglobin was significantly low in SCD as compared to healthy controls [9.1â€‰Â±â€‰1.52 vs. 11.4â€‰Â±â€‰1.04 (p=0.001)]. Mean (% predicted) Forced expiratory volume in 1Â s (FEV1) (86.79â€‰Â±â€‰11.6 vs. 94.3â€‰Â±â€‰16.1) and FVC (84.4â€‰Â±â€‰11.5 vs. 91.75â€‰Â±â€‰15.2) values were significantly low (pâ€‰<â€‰0.001) in cases.Conclusions: The present study revealed that the difference of pulmonary function tests between sickle cell patients and normal age matched controls were statistically significant but this difference was not clinically significant.

58. Ticagrelor versus placebo for the reduction of vasoocclusive crises in pediatric sickle cell disease: Design of a randomized, double-blind, parallel-group, multicenter phase 3 study (HESTIA3)

2018

HemaSphere

Heeney, M M and Abboud, M R and Amilon, C and Andersson, M and Githanga, J and Inusa, B and Kanter, J and Leonsson-Zachrisson, M and Michelson, A D and Berggren, A R and Heeney MM, Abboud M R Amilon C Andersson M Githanga J Inusa B Kanter J Leonsson-Zachrisson M Michelson A D and Berggren, A R and Heeney, M M and Abboud, M R and Amilon, C and Andersson, M and Githanga, J and Inusa, B and Kanter, J and Leonsson-Zachrisson, M and Michelson, A D and Berggren, A R

Background: There is a high unmet need for therapies to reduce the complications of sickle cell disease (SCD), including vaso-occlusive crises (VOCs), in pediatric patients. Activated platelets contribute to the formation of cell aggregates during sickling. Platelet inhibition, therefore, has the potential to reduce VOC rates. Ticagrelor is an oral, direct-acting, and reversible P2Y12 receptor antagonist that inhibits adenosine diphosphate-mediated platelet activation and aggregation. Ticagrelor has a wealth of data in adult cardiac patients and is approved to reduce the rate of cardiovascular death, myocardial infarction (MI), and stroke in adults with acute coronary syndrome (90 mg BID) and adults with a history of MI (60 mg BID). The HESTIA program is currently ongoing to explore the potential therapeutic benefits of ticagrelor for the reduction of VOCs in SCD; the pharmacokinetics (PK), pharmacodynamics (PD), and tolerability of a broad range of ticagrelor doses were investigated in phase 2 studies in children (3-17 y; HESTIA1) and young adults (18-30 y; HESTIA2) with SCD. Though ticagrelor was well tolerated in SCD patients, larger and longer-term studies are needed to assess its safety and ability to reduce VOC rates. Aims: HESTIA3 will evaluate the efficacy, safety, and tolerability of ticagrelor versus placebo over a period of 1 y and up to approximately 2 y in pediatric patients with SCD Methods: Planned enrollment is approximately 182 patients with SCD (randomized 1:1 to receive either ticagrelor or placebo) confirmed for homozygous sickle cell (HbSS) or sickle beta zero thalassemia (HbS/Î²0) and with â‰¥2 VOCs in the year prior to Visit 1 (Figure 1). At least 50 evaluable patients in each age group (â‰¥2 to <12 y and â‰¥12 to <18 y) will be recruited from approximately 20 countries worldwide, including Ghana, Kenya, South Africa, Tanzania, Egypt, Lebanon, Canada, US, Italy, UK, and India. The study drug will be given in addition to standard, locally available treatments for SCD (e.g., stable dose hydroxyurea). Body-weight adjusted ticagrelor doses (15, 30, or 45 mg BID) were identified based on PK/PD modeling and simulation of phase 2 data. The selected ticagrelor doses are projected to achieve greater platelet inhibition than that observed in earlier efficacy trials of platelet inhibition in pediatric SCD. The predicted level of platelet inhibition with the selected doses is â‰¼35% to 80% reduction in P2Y12 reaction units from baseline compared with placebo. Results: The primary endpoint is the number of VOCs (the composite of a painful crisis of â‰¥2 h duration [treated in a medical setting or at home] and/or acute chest syndrome). Secondary endpoints include hospitalizations, symptomatic disease burden, pain intensity and analgesic use during VOCs, acceptability of formulation, and health-related quality of life as measured by the Pediatric Quality of Life Inventory (PedsQL) SCD Module and Fatigue total score and by dimension using the PedsQL Multidimensional Fatigue Scale. Safety will be assessed by adverse events, including bleeding events, and laboratory assessments. Platelet inhibition data, measured by the vasodilator-stimulated phosphoprotein (VASP) assay, will be collected for exploratory purposes. Summary/Conclusion: HESTIA3 will provide long-term data on the effects of ticagrelor in the management of VOCs in pediatric patients with SCD. This trial will target therapeutic platelet inhibition, which is expected to translate into improved clinical results. The first patient is expected to be enrolled during the second quarter of 2018. (Figure Presented).

59. Left ventricular systolic and diastolic functions in patients with sickle cell anemia

2005

Indian Heart Journal

Taksande A, Vilhekar K Jain M and Ganvir, B and Taksande, A and Vilhekar, K and Jain, M and Ganvir, B and Taksande A, Vilhekar K Jain M and Ganvir, B

Background: Sickle cell anemia is a formidable problem in India, and is more prevalent in Maharashtra. Cardiovascular involvement in this condition has not been well studied. The present study therefore sought to investigate the systolic and diastolic left ventricular function of children with sickle cell anemia. Methods and Results: This prospective controlled study comprised of 25 cases of sickle cell anemia, 25 cases of anemia (hemoglobin <11 gm/dl) with 'AA' types of hemoglobin electrophoresis and 25 non-anemic controls (hemoglobin > 11 gm/dl) with normal hemoglobin electrophoresis pattern. M-mode, 2-dimensional and Doppler echcardiographic measurements of patients and controls were performed according to criteria of the American Echocardiography Society. In the study cases, age ranged from 5 years to 15 years with the mean age of 9.91 years. There were 14 males and 11 females in the study cases. Patients with sickle cell anemia had significantly larger left atrial (23.26Â±3.6 mm, 22.9Â±2.56 mm, 20.72Â±2.79 mm; p < 0.05), left ventricular (34.88Â±4.53, 33.28Â±3.28, 30.72Â±3.68; p< 0.05) and aortic root (19Â±2.7, 18.91Â±2.24, 17.56Â±1.44; p<0.05) dimensions. They also had higher indexed end-diastolic left ventricular volumes (101.84Â±22.74 ml/m2 v. 65.05Â±10.81 ml/m2; p< 0.001), and higher stroke volume (29.32Â±11.32 ml, 27.12Â±7.82 ml, 22.4Â±6.67 ml; p<0.05). Left ventricular mass (62.24Â±18.44 gm, 52.53Â±16.23 gm, 50.2Â±15.68 gm; p<0.05) was greater in sickle cell anemia patients than in controls. No statistically significant differences were detected in the Doppler finding of patients with or without anemia. No statistically significant correlation was found between echocardiographic parameters (M-mode and Doppler) and the hemoglobin in the sickle cell patients. Conclusions: Echocardiography is a useful non-invasive technique to study the changes in cardiac structure and function. In spite of left ventricular volume load and dilation in sickle cell anemic patients, left ventricular contraction was good and systolic function was normal, and there was no correlation between the echocardiographic findings and hemoglobin level.

60. Sickle cell anemia in India and Africa

2011

Internet Journal of Hematology

Winters, C

Linguistic archaeological and anthropological evidence suggest that Africans and Indian tribal groups share many features. In this paper we examine the relationship between sickle cell anemia in India and Africa.

61. Unusual stability exhibited by (AT)XN12(AT)Y motif associated with high fetal hemoglobin levels

2019

Journal of Biomolecular Structure and Dynamics

Roy, K and Mahendru, S and Kukreti, R and Kukreti, S

Quasi-palindromic sequences (AT)XN12(AT)Y present in HS2 (hypersensitive site 2) of the human Î²-globin locus are known to be significantly associated with increased fetal hemoglobin (HbF) levels. High HbF levels in some adults arise due to pathological conditions such as sickle cell disease and Î²-thalassemia. However, elevated levels of HbF are also associated with a reducing morbidity and mortality in patients with Î²-thalassemia and thus ameliorate the severity of the disease. Using gel-electrophoresis, ultraviolet (UV)-thermal denaturation, and circular dichroism (CD) techniques, we demonstrated that it exhibits a hairpin-duplex equilibrium. Intramolecular species (hairpin) were observed in both low and high salt concentrations in gel assay studies displaying the unusual

stability of intramolecular species even at the high counter-ion concentration. The unusual stability of hairpin secondary structures was also demonstrated by the monophasic nature of the melting profiles for the oligonucleotides which persisted at low as well as high salt and oligomer concentrations. Change in CD spectra as a function of oligomer concentration indicates that the bimolecular duplex formation is selectively favored over monomolecular hairpin formation at and above 9 ÂµM oligomer concentration. Thus, we hypothesize that imperfect inverted repeat sequence (AT)XN12(AT)Y of HS2 of Î²-globin gene LCR forms the unusually stable hairpins which may result in the formation of a cruciform structure that may be recruited for binding by various nuclear proteins that could result in elevated HbF levels. Communicated by Ramaswamy H. Sarma.

62. Genetic modifiers and severity of sickle cell anemia

2018

International Journal of Laboratory Hematology

Adekile, A

Sickle cell disease (SCD) is an autosomal recessive disease in which homozygotes (SS) have sickle cell anemia while other genotypes e.g. SÎ²-thal, SC, SD are compound heterozygotes. The phenotype is characterized by chronic hemolytic anemia, recurrent vaso-occlusion and vasculopathy. Irrespective of the Hb genotype, the hallmark of SCD is phenotypic variability, driven by genetic and environmental factors. The most recognized genetic modifiers are the Î²S-globin gene haplotype, HbF level and co-existent Î±-thalassemia trait. The haplotype that is associated with the mildest phenotype is the Arab-India haplotype that is characterized by a high level of HbF, which is modulated by cis-acting and trans-acting elements. The former resides primarily in the Xmn-1 C/T restriction site (rs7482144) polymorphism in the 5' HBG2 gene on chromosome 11, while the latter include QTLs in the oncogene, BCL11A on chromosome 2 and the HBS1L-MYB intergenic region on chromosome 6. Other modulators of SCD sub-phenotypes include the UGT1A1 (UDPglucuronyltransferase) polymorphism, which predisposes to hyperbiliriubinemia and gallstones. SNPs in other inflammatory genes and signaling pathways e.g. Annexin II, BMP6 (bone morphogenic protein), TGF-Î² (transforming growth factor) may influence the development of stroke, osteonecrosis, acute chest syndrome etc in SCD.

63. Haemoglobinopathies in nonendemic areas in recent years

2014

Clinical Chemistry and Laboratory Medicine

Frezzotti, A and Galeazzi, M and Paladini, C and Tocchini, M

64. Cardiac state in sickle cell anaemia.

1979

Indian pediatrics

Behera, S K and Swain, U K and Panda, C P and Samal, G C and Mohapatra, S S

65. Increased risk of haematuria and urinary tract infection in sickle cell traits

2012

Journal of Clinical and Diagnostic Research

Pandey, S and Seth, T and Mishra, R M and Saxena, R

66. **Stem Cell Research - Pluripotent Stem Cells; Findings from Rani Durgavati University in Pluripotent Stem Cells Reported (Induced Pluripotent Stem Cell Technology: A Paradigm Shift in Medical Science for Drug Screening and Disease Modeling)**

    2018

    Health & Medicine Week

67. **Severe complications and death in cases of Plasmodium falciparum malaria with sickle-cell trait**

    2005

    Annals of Tropical Medicine and Parasitology

    Pati, S S and Panigrahi, J and Mishra, S K and Mohanty, S and Mohapatra, D N and Das, B S

68. **Restriction endonuclease analysis of DNA in sickle cell lesions among tribals of Bihar, Madhya Pradesh, Gujarat and Rajasthan**

    1989

    Indian Journal of Medical Research - Section B Biomedical Research Other Than Infectious Diseases

    Jain, R C

69. **Delayed Eruption of Teeth in Children with Sickle Cell Haemoglobinopathy in Central India**

    2013

    Indian Journal of Stomatology

Gawande, Madhuri and Agarwal, Priyanka and Chaudhary, Minal and Patil, Swati and Hande, Alka and Gadbail, Amol and Panchbhai, Arti

70. **Protocol for hospital management of dental patients with sickle cell disease**

    2018

    Oral Surgery

    Uppal, N and Janghel, Y

71. **Diverse phenotypic expression of sickle cell hemoglobin C disease in an Indian family**
    2011

    Annals of Hematology

    Patel, D K and Patel, S and Mashon, R S and Dash, P M and Mukherjee, M B

72. **Reproductive wastage in carrier couples of hemoglobinopathies: Experiences from a retrospective study in Madhya Pradesh, India.**

2013

International Journal of Child Health and Human Development

Balgir, Ranbir S and Balgir MSc, PhD, Ranbir S and Balgir, Ranbir S

The beta-thalassemia syndrome and sickle cell disorders are the major genetic and public health challenges in Central India. In view of credit for the 2nd highest infant mortality rate (IMR) in Madhya Pradesh (70 per thousand live-births in 2011), it was presumed that carriers of hemoglobinopathies might be one of the contributing factors for the high IMR. Couples including their offspring with at least one affected/suspected case of hemoglobinopathies, referred to us from NSCB Medical College and Hospital, Jabalpur were consecutively studied as matched case controls. A total of 333 couples were referred during the period from March 2010 to March 2012. Out of 333 couples, 138 were found normal and 195 couples had different hemoglobin disorders. It was observed that the number of conceptions (2.456 vs 1.522), live-births (2.246 vs 1.319), surviving offspring (2.005 vs 1.406), stillbirths (0.082 vs 0.051), and deaths under 10 year (0.236 vs 0.145) were higher and neonatal deaths (0.103 vs 0.116), and deaths under one year (0.118 vs 0.123) per couple at the time of investigations were lower in couples with hemoglobinopathies in comparison to normal controls. It was observed that the frequency of couples with combinations: HbAS x HbAS, HbAS x HbSS, and beta-Thalassemia Trait x beta-Thalassemia Trait, was considerably higher in the under-privileged communities such as scheduled castes (SC) and scheduled tribes (ST), and in Other Backward Castes (OBC) of the state of Madhya Pradesh. Affected families were imparted genetic/marriage counseling. This study indicated that afflicted couples with these hereditary disorders were increasing the affected/carrier offspring. This increased production of defective offspring leads to increased morbidity and mortality and may be contributing towards increased neonatal/infant mortality or fetal wastage in the state of Madhya Pradesh, India. (PsycINFO Database Record (c) 2016 APA, all rights reserved)

73. **To Study The Acute Events In Hospitalized Children Of Sickle Cell Disease**

2018

Pediatric Hematology Oncology Journal

Swapnil wathore and Ajay kasumbiwal

Background & objectives: Children with sickle cell disease require more frequent hospital care and are more vulnerable to mortality. 10 to 15 percent of total hospitalization in pediatric wards at tertiary care are accounted for SCD. There are limited data on the events leading to hospitalizations and death in younger children with sickle cell disease from India. â€¢ Primary objective of this study to evaluate the pattern of acute events in hospitalized children of SCD.â€¢ Secondary objective of my study is to study factors responsible for acute events in hospitalized children of SCD. Methods: Design: This was cross sectional study carried out from Dec 2016 to Aug 2018. Study site paediatric department of a tertiary care hospital in central India. Study population Hospitalized children below 12 years of age with sickle cell disease were enrolled for the study and evaluated for morbid events leading to hospitalization. Haematological indices were noted at the time of hospitalization. these children also evaluated for Immunizations status,hydroxyurea consumption and penicillin prophylaxis. subject with congenital heart disease,congenital anomalies,Malignancy, Tuberculosis and HIV were excluded.96. Results: 245 acute events of hospitalized children of sickle cell disease were enrolled during the study period. Hospitalization with acute painful events (46%) was the most common morbid event followed by severe anaemia (30%) followed by acute febrile illness. Majority (62%) of the events occurred between August and October. Implication & conclusion: acute painful events was the most common morbid event followed by severe anaemia followed by acute febrile illness in hospitalized children with sickle cell disease. There was significant seasonal variation with maximum events occurring in the monsoon season. This study provide pattern of acute events which is important for treatment of morbid events of SCD. Key words sickle cell disease (SCD),acute events,seasonal variation and acute pain full events. Reference 1. Dipty Jain, A.S. Bagul, Maulik Shah & Vijaya Sarathi, Morbidity pattern in

hospitalized under five children with sickle cell disease Indian J Med Res 138, September 2013, pp 317-321 2. Sanjay Tewari & David Rees,morbidity pattern of sickle cell disease in india: a single centre perspective,Indian j med res 138,sept 2013,pp 288-290

74. Morbidity pattern in sickle cell disease in Central Gujarat, India-Single centre perspective 2017

Blood

Bhatwadekar, S S and Deshpande, S V and Khadse, S V and Shah, B and Desai, D

INTRODUCTION: Sickle cell disease (SCD) poses a considerable health burden in India. About 20 per cent of children with SCD die by the age of two and 30 per cent children with SCD among the tribal community die before they reach adulthood is reported in one ICMR survey. As they are vulnerable to mortality, require regular clinical follow up. This retrospective analysis study was, undertaken to evaluate the morbidity pattern in SCD patients observed in patients followed up at our centre METHODS: SCD patients registered and followed up at HOCC between Jan 2011 to June 2017 were included in this study. At first visit to HOCC baseline CBC, PLT, RBC indices, LFT, Creatinine, S.Ferritin,Urine R/M,HPLC pattern,USG abdomen were noted. All 342 patients registered at HOCC were advised to take Hydroxyurea (dose adjusted according to CBC), Folic acid, B12, Multivitamin and Calcium. Vaccination given to selected patients. Out of these 342 patients, 57(16%) patients had 79 hospitalization events, 11 patients (3.2%) had recurrent hospitalizations. All patients were hospitalized in Sterling Hospital Vadodara.CBC PLT,RBC indices,LFT, RFT done on admission in all patients, Blood and urine culture, PS for MP, Dengue NS1,IgG,IgM, in all febrile patients, Viral markers ,CXR,USG Abdomen, MRI pelvis with HIP done in selected patients. All hospitalized patients received adequate hydration by IV fluids.Paracetamol, Contramol, Buprenorphine transdermal patch for pain relief. PCV transfusion to keep HB 8 to 10 gm%.Antibiotics if any evidence of infection, pre-emptive or based on culture report.Oxygen by nasal prongs or NRBM,NIV or Invasive Ventilator support to maintain SPO2 more than 95%.Exchange transfusion if no pain relief in vasoocclusive crisis in 48 hrs or has Acute Chest Syndrome, Splenic Sequestration or Hepatic cell crisis RESULTS: Seventy nine hospitalization events of 57 SCD patients during study period were evaluated to analyse morbidity pattern. Out of 57 patients 47 (82%)patients were not taking regular treatment,10 patients (17%)inspite of regular treatment and follow up developed morbid events .Age range 7 yrs to 57 years, M:F ratio 2:1(Male 38,Female 19),5(8%) patients were pregnant ,Vaso-occlusive crisis was most common morbid event 46(58%) followed by LRTI,ARDS,Acute chest syndrome 9(11%),Hepatic cell crisis 8(10%),Septicemia 6(7.5%),Splenic sequestration 3(3.7%), Aplastic crisis 2(2.5%),Dengue 2(2.5%),Vivax Malaria 2(2.5%),AVN 2(2.5%).Septic arthritis 1(1.2%),Majority of hospitalization observed in month of July and Aug followed by in September ,October, least admissions in the month of April and December,HB F level was more than 20% in 16 patients(28%) and between 10 to 20 % in remaining patients(72%).Duration of hospitalization less than 10 days in majority 69(87%),14 days in 10(12%),Ventilator support was required for 7(8.8%) ,O2 by NRBM in 2(2.5%) ,O2 by nasal prongs 1(1.2%),Blood and Urine Culture for gram negative bacterial growth detected in 6(7.5%),none of the patient had gram positive growth, Exchange transfusion was required for 19 patients(24%) Outcome was favourable in 75(94%),whereas 4 patients(5%) who were not on regular follow up and they reached hospital almost 72 hrs after initial symptoms of crisis succumbed ,Major cause of mortality was Hypoxia, Septicemia with multiorgan failure on day1 of admission in hospital with rapid deterioration within 24 hrs. CONCLUSION: SCD patients on Hydroxyurea and supportive therapy have significantly lower incidence of morbid events requiring hospitalization.Vaso-occlusive crisis is a major reason of hospitalization. Gram negative septicaemia is the leading cause of infective morbidity. Hepatic cell crisis observed predominantly in ethanol addicted patients, Mortality is highest with delayed treatment of ARDS, Acute chest syndrome. Four strong predictors of good outcome are adequate hydration, early control on infection, maintaining adequate oxygenation and early initiation of treatment before organ failure sets in.

75. Assessment of Hearing Loss in Children with Sickle Cell Anemia- A Clinical Study

2019

Journal of Advanced Medical and Dental Sciences Research

Priyanka and Singla, Pritesh

Background: Hearing deficit is described as one of the symptoms which happen because of the cochlear high sensitivity to vessel occlusion which is common in children with sickle cell anemia. The present study was conducted to assess hearing loss in children with sickle cell disease. Materials & Methods: The present study was conducted on 105 children with sickle cell anemia (group I) of both genders. Patients' age 5-16 years were included in the study. Equal number of controls (group II) was also considered in the study. The otolaryngology examination was carried out by ENT surgeon. The pure tone audiometry (PTA) was done by an audiometrician in a sound isolated audiometric room. Results: Out of 105 patients, males were 55 and females were 50. Out of 105 cases, 20 had hearing loss and in control 6 had hearing loss. The difference was significant (P< 0.05). Type of hearing loss was conductive seen in 10 in group I, 3 in group II, sensorineural seen 7 in group I and 2 in group II and mixed seen 5 in group I and 1 in group II. The difference was significant (P< 0.05). Type of hearing loss was mild seen 8 in group I, 2 in group II, moderate seen 4 in group I, 1 in group II, moderate seen 5 in group I, 2 in group II and profound 3 in group I and 1 in group II. Conclusion: Among children with sickle cell anemia, there was more prevalence of hearing loss as compared to control group.

76. Explaining anthropometric variations in sickle cell disease requires a multidimensional approach

2012

Indian Journal of Human Genetics

Mukherjee, Malay and Ghosh, Kanjaksha

[2] Despite the fact that all sickle cell disease (SCD) patients have an identical single base change in their DNA, the severity in the clinical manifestations specially the morbidity and mortality varies between and within different population groups. In a population like India where sickle cell anemia is common along with iron deficiency anemia, [11] there is a possibility that low BMI seen in these children with SCD could have nutritional deficiencies which might have occurred due to inadequate food intake because of poor appetite especially during the vasoocclusive crisis.

77. Association of BCL11A genetic variant (rs11886868) with severity in Î²-thalassaemia major & sickle cell anaemia

2016

The Indian Journal of Medical Research

Dadheech, Sneha and Madhulatha, D and Jainc, Suman and Joseph, James and Jyothy, A and Munshi, Anjana

Background & objectives: The amount of foetal haemoglobin that persists in adulthood affects the clinical severity of haemoglobinopathies including Î²-thalassaemia major and sickle cell anaemia (SCA). The present study was undertaken to analyse Î²-thalassaemia as well as SCA patients for the single nucleotide polymorphism (SNP), rs11886868 (T/C) in BCL11A gene and to evaluate the association between this polymorphism and severity of Î²-thalassaemia major and SCA. Methods: a total of 620 samples (420 Î²-thalassaemia major and 200 SCA cases) were analysed before blood transfusion using basic screening tests like complete blood analysis and osmotic fragility and further confirmed by high performance liquid chromatography (HPLC), amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) and reverse dot blot techniques. All patients were transfusion dependent. Patients with Î²-thalassaemia and SCA were classified into mild, moderate, severe

according to the severity score based on Hb levels, age of onset, age at which patients received their first blood transfusion, the degree of growth retardation and splenectomy. Î²-thalassaemia as well as SCA patients were analysed for the SNP, rs11886868 (T/C) in BCL11A gene and association between this polymorphism and severity of Î²-thalassaemia major as well as SCA was evaluated. Results: There was a significant difference in genotypic and allelic frequencies of BCL11A gene polymorphism between mild and moderate and mild and severe cases in both the groups. A significant (P<0.001) difference was observed in the mean HbF levels between the three genotypes in different severity groups. HbF levels were found to be high in CC genotype bearing individuals followed by TC and TT in Î²-thalassaemia major as well as SCA. Interpretation & conclusions: This study confirms that the T/C variant (rs11886868) of the BCL11A gene causing downregulation of BCL11A gene expression in adult erythroid precursors results in the induction of HbF and ameliorates the severity of Î²-thalassaemia as well as SCA.

78. Modulating effect of the -158 GÎ³ (Câ†'T) Xmn1 polymorphism in indian sickle cell patients

2012

Mediterranean Journal of Hematology and Infectious Diseases

Pandey, S and Pandey, S and Mishra, R M and Saxena, R

Xmn1 polymorphism is a known factor, which increases fetal haemoglobin production. Among the inherited disorders of blood, thalassaemia and Sickle Cell Diseases contributes to a major bulk of genetic diseases in India. Our aim was to verify the role of the Xmn1 polymorphism as a modulating factor in sickle cell patients and frequency of the polymorphism in Indian sickle cell patients. 60 sickle homozygous and 75 sickle beta thalassemia patients were included and 5 ml blood sample was collected from them. Screening of sickle patients was done by HPLC. An automated cell analyzer SYSMEX (K-4500 Model) was used to analyze the Complete Blood Count of patients. Xmn1 polymorphism analysis was done by PCR-RFLP and one-way ANOVA test was applied to analysis of variance between groups. Among the sickle patients 27 were heterozygous (+/-) and 19 were homozygous (+/+) while 30 were heterozygous (+/-) and 24 were homozygous (+/+) in sickle p-thalassemia patients. Extremely significant differences (p-value <0.001) of hematological parameters seen among patients with Xmn1 carrier and without the Xmn1 carrier. In our cases the clinical symptoms were barely visible and higher HbF level with Xmn1 carriers were found. Presence of Xmn1 polymorphism in sickle cell patients with higher HbF were phenotypically distinguished in the sickle cell patients. We conclude that the phenotypes of Indian sickle cell patients were greatly influenced by Xmn1polymorphism.

79. Osteomyelitis in Sickle Cell Disease

1990

Indian Journal of Radiology and Imaging

Ghosh, B P and Samal, S

The present study reports on the clinico-radiological observations in 15 patients of Sickle Cell Disease having extensive long bone involvement. Their ages ranged between 3 and 13 years. All these cases showed a common pattern of diaphyseal changes that helped to establish the diagnosis of Salmonella osteomyelitis.

80. Role of co-inherited Gilbert syndrome on hyperbilirubinemia in Indian beta thalassemia patients.

2014

Hematology (Amsterdam, Netherlands)

Dabke, Pooja S and Colah, Roshan B and Ghosh, Kanjaksha K and Nadkarni, Anita H

BACKGROUND: Gilbert syndrome is characterized by mild unconjugated hyperbilirubinemia. The high levels of bilirubin could be related to the co-inheritance of Gilbert syndrome determined either by mutations of the coding region or by variation in the (TA)n motifs of the promoter region of the bilirubin UGT1A1 gene. The co-inheritance of Gilbert syndrome has been reported to elevate bilirubin levels in beta thalassemia and sickle cell disease patients. Aim In this study, we have tried to investigate whether the variability in serum bilirubin levels found in transfusion-dependent beta thalassemia, beta thalassemia intermedia, and heterozygous beta thalassemia individuals could be related to the coexistence of Gilbert syndrome. METHODS: The promoter region (TA)n motifs of the bilirubin UGT1A1 gene were analyzed in 104 beta thalassemia individuals. The control group consisted of 50 healthy individuals. RESULTS: The analysis of the UGT1A1 promoter showed three (TA) motifs: (TA)5, (TA)6, and (TA)7. The frequency of genotype (TA)7/(TA)7 did not differ significantly between the groups studied. A significant difference was observed in mean serum bilirubin levels between individuals showing (TA)7/(TA)7 and (TA)6/(TA)6 genotypes and also between (TA)7/(TA)7 and (TA)6/(TA)7 genotypes among all groups studied. According to the beta genotype, no differences were observed between mean serum bilirubin levels in the three groups (Î²(+)/Î²(+), Î²(0)/Î²(+), and Î²(0)/Î²(0)). CONCLUSION: These results indicate that the (TA)7/(TA)7 configuration is one of the factors responsible for hyperbilirubinemia and, therefore, seems to interfere with the clinical expression of homozygous beta thalassemia. This emphasizes the role played by co-inherited modifying genes on clinical heterogeneity of monogenic disorders.

81. Evaluation of serum zinc and antioxidant vitamins in adolescent homozygous sickle cell patients in Wardha, district of central India

2017

Journal of Clinical and Diagnostic Research

Wasnik, R R and Akarte, N R

Introduction: Sickle cell anaemia is a condition characterized by haemolytic and vaso occlusive crisis. Previous studies in different part of the world have reported deficiency of zinc, vitamin C and E but the role of their supplementation in sickle cell disease remains question. Nutritional factors may contribute to clinical manifestation in rural population of developing countries specially in adolescent age group. Thus, the present study was designed in rural population of Wardha district of Maharashtra in adolescent sickle cell homozygous patients in view to evaluate serum zinc and antioxidant vitamin C and E. Aim: To evaluate the serum zinc and antioxidant vitamins C and E in cases of adolescent homozygous sickle cell disease. Materials and Methods: The study includes adolescent (between 10-20 years) individuals in two groups of 33 each. Group A included confirmed cases of Sickle Cell Disease (SCD) and Group B included age and sex matched normal healthy controls. Serum zinc, vitamins C and E were analysed in all the subjects of both the groups. Data were expressed as MeanÂ±SD; unpaired t-test was used to compare the two groups. Statistical significance was decided by calculating the p-value. Results: Serum levels of zinc and antioxidant vitamin E and C were significantly low in sickle cell anaemia patients when compared to normal health controls (p-value<0.001). Conclusion: Our study shows that the adolescent patients with SCD have significant low levels of zinc and significantly low antioxidant vitamins C and E, which may contribute to some of the manifestations of sickle cell disease.

82. Hemoglobin Hofu or alpha 2 beta 2 [126 (H4) Va1 leads to Glu] found in combination with hemoglobin S.

1978

Hemoglobin

Brittenham, G and Lozoff, B and Harris, J W and Nayudu, N V and Gravely, M and Wilson, J B and Lam, H and Huisman, T H

Hb Hofu, alpha 2 beta 2 [126 (H4) Va1 leads to Glu], was found in 10 members of 2 apparently unrelated Valmiki families in central India. None showed evidence of hemolysis and hemoglobin levels were normal in most. In two

individuals, Hb Hofu occurred in combination with Hg S, but neither had clinical manifestations of sickle cell disease. In samples containing Hb Hofu, the isopropanol precipitation test was positive. Quantitation of the hemoglobin fractions by DEAE-cellulose chromatography showed that Hb Hofu constituted a mean of 23--25% of the total whether in combination with Hb A or Hb S.

83. Hb F Levels in Indian Sickle Cell Patients and Association with the HBB Locus Variant rs10128556 (C>T), and the HBG XmnI (Arab-Indian) Variant

2017

Hemoglobin

Bhanushali, A A and Himani, K and Patra, P K and Das, B R

The prevalence of sickle cell disease in India is very high. Hb F is one of the most powerful modulators of disease severity in sickle cell disease patients. It was traditionally thought that the disease is milder in Indian sickle cell disease patients predominantly due to the Arab-Indian haplotype characterized by the HBG XmnI [rs7482144 (G>A)] variant, which is associated with increased Hb F levels. In the current study, we investigated the Hb F levels in individuals with the rs10128556 (C>T) variant and also determined its linkage with the HBG XmnI variant. The present study was conducted on a cohort of 275 individuals, which consisted of 221 patients with sickle cell disease and 54 patients with sickle cell trait. Analysis of hemoglobin (Hb) fractions and variants was done on the high performance liquid chromatography (HPLC) system. Genotyping for rs10128556 was done by direct sequencing of the products. Mean Hb F levels in the sickle cell disease patients was 19.36 Â± 6.79. The genotypic frequencies for rs10128556 were 82.0% (TT), 16.7% (CT) and 1.3% (CC) for sickle cell disease patients. The minor C allele resulted in 52.0% decrease in Hb F levels when homozygous and 7.0% decrease when heterozygous. The rs10128556 single nucleotide polymorphism (SNP) was in strong but not complete linkage with the HBG XmnI variant. In conclusion, the study determined for the first time the frequency and association of rs10128556 in Indian sickle cell disease patients with Hb F. It also established that it was not in complete linkage with the HBG XmnI variant in this high risk population.

84. Phenotypic expression of HbO indonesia in two indian families and its interaction with sickle hemoglobin (HbS)

2016

Indian Journal of Hematology and Blood Transfusion

Kainaz, S and Amar, D G and Anita, N and Pallavi, M and Manju, G and Manisha, R and Pradnya, C and Vishal, M and Roshan, C

Background: Alpha globin chain variants are clinically significant since they directly influence the structure and function of the hemoglobin (Hb) molecules they constitute, either in combination with normal beta globin chains or with variant beta chains, thereby altering the morbidity and mortality associated with the resultant hemoglobinopathies. We describe here two unrelated families from Madhya Pradesh who had a non-deletional alpha chain variant, HbO Indonesia [CD 116 Gâ†'A]. Members of one of the two families also had coinheritance of HbS. Aims: To study the phenotype of HbO Indonesia and its interaction with HbS. Material and Methods: Hb electrophoresis, High performance liquid chromatography (HPLC), Covalent reverse dot blot hybridization, Amplification refractory mutation system, Multiplex PCR and direct gene sequencing were used to identify and characterize the variant Hbs. Results: The abnormal hemoglobin moved with HbS in Hb electrophoresis at alkaline pH and gave an abnormal peak in HPLC with a retention time of 4.86-4.89 minutes. In two members of the family with coinheritance of HbS it produced small additional abnormal Hb peaks (4.6 % in heterozygous and 11.9 % in homozygous member) in HPLC with a longer retention time (5.15-5.17 minutes) possibly resulting from a combination of HbO Indonesia alpha chain with HbS beta chain. Conclusions: It appears that depending on the zygosity of HbS, HbO Indonesia would subtract a variable amount of HbS beta chain from the total pool thereby

potentially reducing the clinical severity of HbS disease. HbO Indonesia per se does not cause anemia or alter the red cell indices.

85. Estimation of iron status in paediatric patients with beta thalassemia and sickle cell disease

2015

Indian Journal of Clinical Biochemistry

Sarma, N and Teli, A B and Baruah, A

Blood transfusion is the mainstay of supportive treatment in patients with thalassemia and sickle cell disease which is lifesaving at the same time can cause overt side effects. We investigate iron status and find correlation with number of blood transfusions in patients with thalassemia and sickle cell disease. This comparative study is carried out in the Paediatrics department and lab investigations being carried out in the clinical biochemistry laboratory and RIA center for one year. 30 cases of thalassemia and 30 cases of sickle cell disease were enrolled for study. Serum iron and TIBC estimated in semi-autoanalyzer by colorimetric method and ferritin estimated by radioimmunoassay method. In patients with thalassemia mean Â± S.D. of iron, TIBC and ferritin found to be 184.73 Â± 26.96, 235 Â± 33.39, 1103.16 Â± 450.26 and in sickle cell disease this results are 148.36 Â± 24.16, 221.16 Â± 56.29, 673.34 Â± 356.26 respectively. There is statistically significant positive correlation of number of transfusion with ferritin in both group of patients ($p<0.05$). Estimation of iron status is important in transfusion dependent patients as management for iron overload and its untoward effect can be done at the earliest with proper monitoring.

86. Analysis of sickle cell gene using polymerase chain reaction and restriction enzyme Bsu 361
1995

Indian Journal of Medical Research

Husain, S M and Kalavathi, P and Anandaraj, M.P.J.S.

A 772bp DNA fragment from human Î²-globin gene has been amplified by polymerase chain reaction (PCR) and subjected to restriction enzyme analysis using Î²su 361, an isoschizomer of restriction enzyme Mst II. This protocol has been designed basically to enhance the analytical facility for the detection of sickle cell mutation. A 430bp DNA fragment was found to be associated with the mutant locus, whereas 228bp and 202bp DNA fragments were generated from the normal locus. This difference of about 202bp in the resulting fragments from the mutant and normal loci has improved discriminatory power in the genotype analysis of the sickle cell mutation.

87. Development of a specific solubility test to identify separately haemoglobin s and non-HBS sickling haemoglobins

2011

Clinical Chemistry and Laboratory Medicine

Agrawal, U and Mittal, R and Palandurkar, K and Goyal, M M and Basak, A

Background. Sickle cell disease (SCD) is prevalent in many countries of the world. Haemoglobin (Hb) electrophoresis is not feasible as a routine diagnostic test for SCD. Modifications of Solubility test during 1970 - 1972 failed to distinguish HbS and non- HbS sickling Hb in our laboratory. Hence, this study was initiated to modify solubility reagent to develop a specific Solubility test. Methods. Diagnosis of SCD was done by Na-metabisulphite Sickling slide test and haemoglobinopathies by Cellulose Acetate Membrane (CAM), Citrate-Agarose Acid electrophoresis & native-PAGE. We modified the Solubility reagent and the test described in literatures in respect to molarity, pH, concentrations of saponin, Na-dithionite, urea and Hb. Results. We screened 2461 patients by Sickling slide test and 107 SCD cases (4.01%) were diagnosed as SCD. The same cases were also identified positive by our modified Solubility test. Out of these, 40(37.4%) were HbS and 67 were non-HbS

sickling Hbs (62.7%). Electrophoretogram of non-HbS sickling Hb and HbS in CAM & native-PAGE were same, but in Citrate-Agarose acid electrophoresis all the 40 cases of HbS & 67 cases of non-HbS could be resolved by slightly lesser migration of non-HbS. Sensitivity and specificity of our developed Solubility test to detect HbS and non-HbS sickling Hb were 100%, in comparison to gold standard Citrate-Agarose acid electrophoresis. Conclusions. We could successfully modify the Solubility test to distinguish HbS and non-HbS sickling Hb and as a result, the predominance of non-HbS sickling haemoglobinopathies could be reported first time in Vidarbha region of Maharashtra State, India.

88. Application of continuous-wave photoacoustic sensing to red blood cell morphology

2019

Lasers in Medical Science

Gorey, Abhijeet and Biswas, Deblina and Kumari, Anshu and Gupta, Sharad and Sharma, Norman and Chen, George C K and Vasudevan, Srivathsan

The feasibility of continuous wave laser-based photoacoustic (CWPA) response technique in detecting the morphological changes in cells during the biological studies, through the features extracted from CWPA signal (i.e., amplitude) is demonstrated here. Various hematological disorders (e.g., sickle cell anemia, thalesemia) produce distinct changes at the cellular level morphologically. In order to explore the photoacoustic response technique to detect these morphological changes, we have applied CWPA technique onto the blood samples. Results of our preliminary study show a distinct change in the signal amplitude of photoacoustic (PA) signal due to a change in the concentration of blood, which signifies the sensitivity of the technique towards red blood cell (RBC) count (related to hematological disease like anemia). Further hypotonic and hypertonic solutions were induced in blood to produce morphological changes in RBCs (i.e., swollen and shrink, respectively) as compared to the normal RBCs. Experiments were performed using continuous wave laser-based photoacoustic response technique to verify the morphological changes in these RBCs. A distinct change in the PA signal amplitude was found for the distinct nature of RBCs (swollen, shrink, and normal). Thus, this can serve as a diagnostic signature for different biological studies based on morphological changes at cellular level. The experiments were also performed using conventional pulsed laser photoacoustic response technique which uses nano-second pulsed laser and the results obtained from both PA techniques were validated to produce identical changes. This demonstrates the utility of continuous wave laser-based photoacoustic technique for different biological studies related to morphological cellular disorders.

89. Effect of inherited red cell defects on growth of Plasmodium falciparum: An in vitro study

2018

The Indian Journal of Medical Research

Pathak, Vrushali and Colah, Roshan and Ghosh, Kanjaksha

Background & objectives: High prevalence of certain polymorphic alleles of erythrocytes in malaria endemic area has been linked to the resistance provided by these alleles against parasitic infestations. Numerous studies undertaken to demonstrate this correlation have generated conflicting results. This study was undertaken to investigate the abilities of various polymorphic erythrocytes to support in vitro growth of Plasmodium falciparum parasites. Methods: In this study under in vitro condition the ability of P. falciparum parasites to grow was assessed in the erythrocytes obtained from a total of 40 patients with various haemoglobinopathies, such as Î²-thalassaemia (Î²-Thal), sickle cell anaemia, erythroenzymopathy-like glucose-6-phosphate dehydrogenase deficiency and membranopathy-like hereditary spherocytosis. Results: Significantly reduced in vitro invasion and growth of parasites was seen in the cultures containing abnormal erythrocytes than in control cultures containing normal erythrocytes (P< 0.05). The mean per cent parasitaemia comparison was also carried out among the three polymorphic erythrocyte groups, i.e. Î²-Thal, sickle cell anaemia and enzyme-membranopathies. Interpretation & conclusions: Erythroenzymopathies and membranopathies were found to provide a more hostile environment for

parasites, as the least parasitaemia was observed in these erythrocytes. The present in vitro study showed that P. falciparum did not grow well and did not invade well in erythrocytes obtained from common inherited red cell disorders.

90. Genetic variant in the BCL11A (rs1427407), but not HBS1-MYB (rs6934903) loci associate with fetal hemoglobin levels in Indian sickle cell disease patients

2015

Blood Cells, Molecules, and Diseases

Bhanushali, A A and Patra, P K and Nair, D and Verma, H and Das, B R

India along with Nigeria and DRC contribute to 57% of the world sickle cell anemia population. The annual number of newborns in India with SCA was estimated at 44,000 in 2010. Even with this high prevalence there is minimal information about genetic factors that influence the disease course in Indian patients. The current study was conducted on 240 patients with SCD and 60 with sickle cell trait, to determine the association of genetic variants at the BCL11A (rs1427407) and HBS1-MYB (rs6934903) loci with fetal hemoglobin levels (HbF). Both these loci have been implicated with influencing HbF levels, a powerful modulator of the clinical and hematologic features of SCD.Our results indicate the BCL11A rs1427407 G. >. T variant to be significantly associated with HbF levels {19.12. Â±. 6.61 (GG), 20.27. Â±. 6.92 (GT) and 24.83. Â±. 2.92 (TT) respectively} contributing to ~. 23% of the trait variance. Interestingly no association of the HBS1L-MYB rs6934903 with the HbF levels was seen.The present study indicates the BCL11A (rs1427407) but not HMIP (rs6934903) to be associated with elevated HbF levels in Indian patient. Further interrogation of additional variants at both the loci; as also a GWAS which may help uncover new loci controlling HbF levels.

91. Genotyping of alpha-thalassemia in microcytic hypochromic anemia patients from North India.

2006

Journal of applied genetics

Sankar, Vaikam H and Arya, Vandana and Tewari, Depshikha and Gupta, Usha R and Pradhan, Mandakini and Agarwal, Sarita

Microcytic hypochromic anemia is a common condition in clinical practice and alpha-thalassemia has to be considered as a differential diagnosis. Molecular diagnosis of alpha-thalassemia is possible by polymerase chain reaction. The aim of this study was to evaluate the frequency of alpha-gene numbers in subjects with microcytosis. In total, 276 subjects with microcytic hypochromic anemia [MCV<80fl; MCH<27pg] were studied. These include 125 with thalassemia trait, 48 with thalassemia major, 26 with sickle-cell thalassemia, 15 with E beta-thalassemia, 40 with iron-deficiency anemia, 8 with another hemolytic anemia, and 14 patients with no definite diagnosis. Genotyping for -alpha3.7 deletion, -alpha4.2 deletion, Hb Constant Spring, and a-triplications was done with polymerase chain reaction. The overall frequency of -alpha3.7 deletion in 276 individuals is 12.7%. The calculated allele frequency for a-thalassemia is 0.09. The subgroup analysis showed that co-inheritance of a-deletion is more frequent with the sickle-cell mutation than in other groups. We were able to diagnose 1/3 of unexplained cases of microcytosis as a-thalassemia carriers. The a-gene mutation is quite common in the Indian subcontinent. Molecular genotyping of a-thalassemia helps to diagnose unexplained microcytosis, and thus prevents unnecessary iron supplementation.

92. Sample dilution to resolve mistaken identification of haemoglobin D as haemoglobin E using the variant automated system

1998

Journal of Clinical Pathology

Thomas, S

High performance liquid chromatography (HPLC) is increasingly being used to estimate variant haemoglobins. A case of haemoglobin S/D (HbS/D) is presented, which was misdiagnosed as haemoglobin S/E (HbS/E) by HPLC. The patient was a 22 year old woman with sickle cell anaemia. Subsequent haemodilution by blood transfusion clearly elucidated the haemoglobin D peak on HPLC. Sample dilution experiments, using the pretransfusion sample, were done resulting in correct elution of the peak in the D window. Troubleshooting in similar problematic haemoglobin variant peaks seen on HPLC can be done by sample dilution.

93. Poor Health Related Quality of Life Among Patients of Sickle Cell Disease.

2014

Indian Journal of Palliative Care

Bhagat, Vijay M and Baviskar, Shubhangi R and Mudey, Abhay B and Goyal, Ramchandra C

Background: Sickle cell disease (SCD) is characterized by chronic hemolytic anemia and vascular occlusion, causing recurrent painful episodes, neuro-cognitive deficits, organ failures and death in early adulthood. Besides the medical consequences, most of the families with a child of SCD have to cope with financial and social crisis. Quality of life (QOL) is a broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life. Other than health; emotional well being, social dysfunction, chronic pain and fatigability are also important aspects of overall quality of life that add to the complexity of its measurement. Aim: The present case control study was designed to determine the health related quality of life (HRQoL) in patients of sickle cell disease and to compare it with patients of other chronic non-communicable diseases. Setting and Design: Case control study conducted at tertiary health care facility of Central India. Material and Methods: The present study conducted to measure HRQoL among patients of SCD and patients of other chronic non-communicable diseases. A translated and pretested version of WHO SF-36 questionnaire was used to measure HRQoL. Results: We observed that there was significantly lower HRQoL among SCD patients. Conclusion: Besides merely pharmacotherapy, restoration of overall quality of life should be the mainstay of management of patients with SCD.

94. The Bone Pain Crisis of Sickle Cell Disease and Malaria: Observations from Gujarat, India.
2017

Indian Journal of Community Medicine

Patel, Jyotish and Patel, Bharati and Serjeant, Graham R

Background: Sickle cell disease is a common problem across central India, but its clinical features may differ from that in African populations. There is a need to define the features of sickle cell disease in India, and the current study addresses some features of the bone pain crisis. Objectives: The objective of the study was to describe the epidemiology of the bone pain crisis of sickle cell disease in Gujarat and explore the relationship with infection by Plasmodium vivax. Materials and Methods: This was a prospective review of all admissions in patients with sickle cell disease to a private pediatric institution in Bardoli, Gujarat, in the year 2015. Hemoglobin electrophoresis of all patients was consistent with homozygous sickle cell disease, but family studies indicated that at least seven cases had the severe sickle cell-beta + thalassemia presumed to be the common IVS1-5G>C mutation. Clinical, hematological, and parasitological features were recorded. Results: There were 914 admissions among 654 patients who had between one and seven admissions. The bone pain crisis accounted for 763 (83%) of admissions and increased between July and October coinciding with the monsoon period. Blood smears were examined for malarial parasites in 811 admissions and were positive for P. vivax in 73% patients. There was no evidence that P. vivax infections varied with the cause of admission or increased during the monsoon period. Conclusions: There was a high prevalence of P. vivax infection in hospital admissions of sickle cell patients, but the data did not support an etiological role in the bone pain crisis. A trial of malarial prophylaxis might determine its effect on the clinical features and outcome of sickle cell disease.

95. **Structure-activity relationship of heme and its analogues in membrane damage and inhibition of fusion**

    2018

    FEBS Letters

    Das, D and Tarafdar, P K and Chakrabarti, A

Under pathological conditions, such as sickle cell disease and malaria, heme concentration increases considerably, and it induces membrane damage. As sickled and normal erythrocytes contain high cholesterol: phospholipid ratio, we investigated the role of lipid composition, chain length, and unsaturation on the partitioning and leakage of hemin in phospholipid vesicles. To establish structure-activity relationship in membrane damage, experiments with two other analogues, protoporphyrin-IX and hematoporphyrin (HP) were also carried out. Hemin and its analogues localize differently in membranes and exhibit distinct roles in partitioning, leakage and fusion. Hemin and HP trigger more leakage in the presence of aminophospholipids, whereas cholesterol buffers the destabilizing effect remarkably. Inhibition of fusion by hemin further suggests its unexplored and important role in membrane trafficking, particularly under diseased conditions.

96. **282.64 Sickle-cell/HB-C disease with crisis**

    2011

    Hospital Inpatient Profiles

97. **Sickling as a cause of bilateral avascular necrosis of hip with autoinfarction of spleen**

    2003

    Indian Journal of Radiology and Imaging

    Shash, H R and Patwa, P C and Tannk, A V and Jindal, N and Hans, D and Nayak, C

98. **Priapism in children with sickle-cell disease.**

    1992

    Indian pediatrics

    Enwerem, E O and Endeley, E M and Holcombe, C and Patel, R V

99. **Can inequity in healthcare be bridged in LMICs â€“ Multicentre experience from thalassemia day care centres in India**

    2017

    Pediatric Hematology Oncology Journal

Parmar, L and Sedai, A and Ankita, K and Dhanya, R and Agarwal, R K and Dhimal, S and Shriniwas, R and Iyer, H V and Gowda, A and Gujjal, P and Pushpa, H and Jain, S and Kondaveeti, S and Dasaratha Ramaiah, J and Raviteja and Jali, S and Tallur, N R and Ramprakash, S and Faulkner, L

100.Intrahepatic calculi in sickle cell anaemia.

1997

The Journal of the Association of Physicians of India

Namjoshi, S P

101.Rare splenic manifestations of sickle cell disease

2002

Indian Journal of Radiology and Imaging

Mohanty, J and Bhagat, S and Panda, B B and Pappachan, B

102.Hepatic sequestration of red cells in sickle cell anaemia.

1987

The Journal of the Association of Physicians of India

Sarma, P S

103.Recessive congenital methemoglobinemia due to NADH-cytochrome b5 reductase deficiency associated with recurrent early pregnancy loss (REPL) in an Indian family

2012

Annals of Hematology

Kedar, Prabhakar and Warang, Prashant and Ghosh, Kanjaksha and Colah, Roshan

104.Three genetic markers and malaria in upper caste hindus of Kheda District of Gujarat State.

1993

Indian journal of malariology

Pant, C S and Gupta, D K and Bhatt, R M and Gautam, A S and Sharma, R C

105.De novo heterozygous Hb G-Waimanalo (Î±64(E13)Asp>Asn, CTG>CCG; HBA1:c.193G>A) variant in a sickle cell disease patient of an Indian tribe

2021

Journal of Clinical Pathology

Kumar, R and Mishra, S and Uikey, R S and Gwal, A and Mun, A and Bharti, P K and Shanmugam,R

106.Osteonecrosis and leg ulceration in Indian sickle cell patients.

2012

Indian Journal of Pediatrics

Pandey, S and RM, Mishra and Saxena, R and Pandey, Sanjay and Mishra, R M and Saxena, Renu

ODISHA

PREVALENCE

1. **Factors responsible for mortality in patients with sickle cell disease: A hospital-based study**

2020

National Journal of Physiology, Pharmacy and Pharmacology

Purohit, P and Mantri, S and Nayak, J and Mahapatra, B and Purohit1, Prasanta and Mantri1, Satwana and Nayak2, Jayanti and Mahapatra3, Bibhupada and Purohit, P and Mantri, S and Nayak, J and Mahapatra, B and Purohit1, Prasanta and Mantri1, Satwana and Nayak2, Jayanti and Mahapatra3, Bibhupada

Background: Sickle cell disease is the most common hemoglobin disorders in the state of Odisha with a significant morbidity and mortality. Various factors are responsible for the mortality in patients with sickle cell disease. Aims and Objectives: This study was undertaken to explicate the possible cause of mortality in patients with sickle cell disease hospitalized in a tertiary health-care facility. Materials and Methods: From June 2017 to December 2018, 22 hospitalized sickle cell disease patients had died. All the demographic, hematological, and clinical investigations of the deceased patients were compared with age- and gender-matched hospitalized sickle cell disease patients who survived and were discharged during this study period. All the demographic features, hematological, and clinical investigations were compared in both the deceased and survived patients. The Statistical Package for the Social Sciences version 16.0 software was used for all possible statistical analyses and P< 0.05 was considered as statistically significant. Results: Majority of the deceased patients were belonging to rural area (90.19%) which was significantly high (P = 0.0271) compared to survived patients (61.36%). Further, 77.27% of deceased patients were referred from primary health centers compared to 29.55% of patients in survived group (P = 0.0007). All the hematological and clinical parameters were comparable in both the groups. Conclusion: There was a high risk of mortality in patients with sickle cell disease who either referred from other primary health centers and/or belonging to the rural area. An early diagnosis of sickle cell disease, choose of suitable antibiotics, and other therapeutic strategies in hospitalized sickle cell disease patients may combat the disease severity as well as mortality.

2. **Spectrum of Hemoglobinopathies: A New Revelation in a Tertiary Care Hospital of Odisha**

2018

Indian Journal of Hematology and Blood Transfusion

Ray, Gopal Krushna and Jena, Rabindra Kumar

The prevalence of different types of hemoglobinopathies and its spectrum in Odisha state is believed to be high, but its exact prevalence is not known due to lack of large population based study. The present study was undertaken to know the magnitude and spectrum of hemoglobinopathies among the patients attending tertiary care centre for evaluation of anemia. All the patients of various age group without any history of blood transfusion preceding 3Â months of period attending the Clinical Hematology Department of SCB Medical College, Cuttack for evaluation of anemia were included in this 10Â year prospective study. Detail history, clinical examination followed by blood sample examination including by HPLC/CzE were done in all cases. Other investigations were done as per need of evaluation of anemia. Out of 21,371 patients with anemia, hemoglobinopathies was detected in 10,745 (50.2%) cases. The profile of hemoglobinopathy was as follows: HbS gene in 52.48% cases, betathalassemia in 54.06% and HbE hemoglobinopathies in 9.19% cases. Hemoglobinopathy was detected in very high percentage (50.2%) of cases in our centre. Various types of Î²-thalassemia and sickle cell hemoglobinopathies

were two major types (54.06% and 52.48% respectively). This needs to be confirmed by large population based study.

3. **Incidence of hematological malignancies in sickle cell patients from an indian tertiary care teaching hospital**

   2018

   Asian Journal of Pharmaceutical and Clinical Research

   Chauhan, S and Swain, S K and Sahu, M C

Objective: Sickle cell disease (SCD) involves multiple systems and is manifested by variable degree of anemia, acute vaso-occlusive episodes, and chronic organ damage. Small case series have hinted at increased incidence of cancer among SCD patients, but no examination of population-based data in Odisha has been reported. Here, we have reported the association of hematological malignancies and SCD in our region. Methods: In this prospective study, we have documented all the demographic and clinical data of sickle cell patients during the past 3 years from June 2013 to May 2016. Simultaneously, the bone marrow (BM) aspiration and biopsy were carried out for all patients. This study was approved from the Institutional Ethics Committee. Results: A total number of 267 sickle cell patients were screened for malignancy by both BM aspiration and biopsy. Among them, 6 cases of malignancies were detected by both BM aspiration and biopsy method. Conclusion: Our study shows a association between SCD and hematological malignancies which could be due to treatment with hydroxyurea or accumulation of multiple genetic abnormalities due to a high degree of proliferative activity of marrow cells.

4. **Influence of sickle cell gene on Plasmodium falciparum MSP-1 and 2 alleles in symptomatic malaria**

   2009

   Indian Journal of Hematology and Blood Transfusion

   Mashon, R S and Patel, D K and Patel, S and Dash, P M

Background: Malaria exerts selective pressure on various human hemoglobin variant and as a corollary, these Hb variants affect the prevalence to distinct Plasmodium falciparum genotypes (MSP1 and 2). Many of the studies on asymptomatic malaria infections have supported this theory. While a lone study carried out in symptomatic malaria has reported a limited influence of sickle gene. Aim: Assess the influence of sickle cell gene on the prevalence and multiplicity of Plasmodium falciparum infection (MSP-1 and 2 allele) in symptomatic malaria cases. Methodology: The study was conducted at V.S.S. Medical College Hospital, Orissa, India and approved by the Institutional Ethical Committee. Sixty adult symptomatic malaria cases were recruited in three groups Hb AA (n = 25), AS (n = 18) and SS (n = 17) from July 2006 to August 2007. Genotyping of peripheral blood P. falciparum parasites for MSP-1 (K1, MAD20 and R033 allele) and MSP-2 (3D7 and FC27) gene was done by Nested PCR. Multiplicity of infection (MOI) and Multiclonal infection was calculated from the band pattern obtained. ANOVA and trend test were used as required. Results: MOI was significantly different for MSP-1 allele (ANOVA p = 0.04), while it was comparable for MSP-2 allele in the three groups. K1 and MAD20 allele showed a significant decreasing prevalence, X2 trend 7.25 and 6.17; and p-value 0.007 and 0.01 respectively in HbAA, AS and SS cases, while no significant trend was observed for R033, 3D7 and FC27 alleles. Polyclonal infections were present significantly high for MSP1 isolates in HbAA (88%) type as compared to AS (40%) and SS (37.5) variants (X2 trend =10.4; p=0.001), while no such trend was observed for MSP2 where multiclonal isolates were AA (50%), AS (18.2%) and SS (40%). Conclusion: The sickle cell gene influences the prevalence of selective alleles and multiplicity of P.falciparum genotypes in symptomatic malaria.

5. **Ophthalmic manifestation of sickle cell patients in eastern India**

   2018

   Journal of Clinical and Diagnostic Research

   Samant, S and Dhar, S K and Sahu, M C

Introduction: Sickle Cell Disease (SCD) is the most common and serious form of an inherited blood disorder that leads to increased risk of early mortality and morbidity. Some of the ophthalmological complications of SCD include retinal changes, vitreous haemorrhage, and abnormalities of the conjunctiva. Irrecoverable Vision loss may be a manifestation if not diagnosed early and treated appropriately. Aim: To determine different ophthalmic manifestations in SCD patients and correlate in relation to HbS window. Materials and Methods: A total of 49 cases of sickle cell disease (HbSS) that presented to IMS & SUM Hospital were evaluated for ophthalmic manifestations in Ophthalmology OPD with comprehensive eye examination, slit lamp examination, Fundoscopy (Direct and Indirect) and OCT (Optical Coherence Tomography). Demographics and pattern of presentation were recorded in the proforma prepared for the study. Results: Male:Female ratio was 3:1. About 2/3rd of the patients were below 40 years of age. Examination of posterior segment revealed 5 (10%) of the patients presented with proliferative retinopathy, 15 (30%) with non proliferative retinopathy, 13(26%) with optic disc changes, 7 (14%) with retinal macular changes and 2 (4%) had retinal detachment findings are significantly different at p=0.001 in ANOVA Test. Anterior segment of eye evaluation demonstrated significant (p=0.0001) changes 18 (36%) patients suffered conjuctival vascular changes, Cataract in 8(16%) patients, and hyphema in only 2 (4%) patients. Both anterior and posterior segment manifestations significantly (p=0.0027) increased with progressive increase in HbS window. Conclusion: Sickle cell patients need periodic ophthalmic examinations to identify treatable lesions amenable to intervention and to prevent blindness. Both anterior and posterior segment manifestations increases with progressive increase in HbS window in HbSS patients.

6. **Molecular variants and clinical importance of Î²-thalassaemia traits found in the state of Orissa, India**

   2009

   Hematology

   Nishank, S S and Ranjit, M and Kar, S K and Chhotray, G P

Prevention of Î² thalassaemia implies knowledge of the molecular spectrum occurring in the population at risk. This knowledge is necessary, especially when a prevention protocol is applied to a multiethnic population. For this purpose, we carried out molecular analysis of 431 Î² thalassaemia subjects belonging to tribal (aboriginal) and non-tribal communities of Orissa, a part of peninsular India and found six types of mutation (four previously unreported and two reported). Molecular analysis of Î² gene mutation showed that out of 431 Î² thalassaemia cases (265 Î² thalassaemia traits, 64 Î² thalassaemia major, 47 haemoglobin E-Î² thalassaemia, 55 haemoglobin S-Î² thalassaemia cases), 71% of cases (n=306) showed the IVS I-5(Gâ†'C)mutation, 12% of cases (n=52) showed FS 41/42(-CTTT), 7% of cases (n=30) showed CD 15(Gâ†'A), 4Â·8% of cases (n=21) showed CD 30 (Gâ†'C), 3%of cases (n=13) showedFS8/9 (+G), and 2%of cases (n=9) showed IVSI-1(Gâ†'T). The tribal populations possess only the IVS I-5(Gâ†'C) mutation whereas the non-tribal groups possess the FS 41/42(-CTTT), FS 8/9 (+G), IVS I-1(Gâ†'T), CD30(Gâ†'C) and IVS I-5(Gâ†'C)mutations. Among the non-tribal communities,Muslims did not have the IVS I-1 (Gâ†'T)mutation. Clinically, anaemia was mild to moderate in Î² thalassaemia trait and was found to be associated with the majority of abnormalities such as pyrexial episodes, fatigue, headache, lethargy and pallor. However, there were no differences in the incidence of clinical abnormalities between tribal and non-tribal populations and also among the different molecular variants of Î² gene. This is the first report from Orissa on the prevalence of different molecular variants of Î² thalassaemia. The clinical presentation of Î² thalassaemia trait cases and their variation from other population have been discussed with reference to the different genetic variants. Â© 2009 W. S. Maney & Son Ltd.

7. **Clinical and pathological status of haemoglobinopathies among pregnant women in southern Orissa**

   2009

   Indian Journal of Biotechnology

   Panda, A and Praveen, B and Bisht, S S

Sixty-two pregnant women were categorized into four age groups and investigated to know the prevalence of haemoglobinopathies among them in and around Berhampur using sickling test, naked eye single tube red cell osmotic fragility test (NESTROFT), and haemoglobin electrophoresis. Out of the 62 pregnant women four cases of sickle cell trait and one of Î²-thalassaemia trait was found. There was no significant difference recorded in the blood cell indices between normal and sickle cell trait in pregnant women. Sickle cell haemoglobinopathy is prevalent among the general, scheduled caste followed by other backward class groups of southern Orissa and less HbS% was observed among the pregnant women which indicate the probable interaction of sickle hemoglobin with Î±-thalassemia.

8. **Sickle cell-Î²+ thalassaemia in Orissa State, India**

   1991

   British Journal of Haematology

   Kulozik, A E and Bail, S and Kar, B C and Serjeant, B E and Serjeant, G E

The clinical, haematological, and some molecular genetic features of 17 Orissan Indian patients with sickle cell-Î²+ thalassaemia (SÎ²+ thal) are described and compared with those in 131 Indian patients with homozygous sickle cell (SS) disease. Patients with SÎ²+ thal had higher Hb A2 levels, and lower mean cell volume (MCV) and mean cell haemoglobin (MCH) compared to SS disease but no other haematological difference of statistical significance. High levels of Hb F occurred in both genotypes and the Î±+ thalassaemia gene frequency reached 0.47 in SÎ²+ thal and 0.32 in SS disease. Clinically there were no significant differences between the genotypes indicating that the low levels of HbA (3-5%) in this condition were insufficient to modify the clinical features. The thalassaemic Î² globin gene is inactivated by a G â†' C mutation at position 5 of the first intron of the Î² globin gene (IVS1-5 G â†' C) in all cases. This finding should facilitate the introduction of a prenatal diagnosis programme aimed at the prevention of Î² thalassaemia or SÎ²+ thalassaemia in that population.

9. **Spectrum of hemoglobinopathies in Orissa, India**

   2004

   Hemoglobin

   Chhotray, G P and Dash, B P and Ranjit, M

Five hundred and 20 cases (279 males; 241 females), referred for anemia, with a wide age range, from different parts of the state of Orissa, India, were investigated to evaluate the extent of the prevalence of hemoglobinopathies (sickle cell disorders and thalassemias) by analyzing the associated hemoglobin (Hb) profiles, Hb genotypes, as well as the clinical and hematological parameters. We found sickle cell trait (Hb AS) in 131 cases (62 males; 69 females), homozygous sickle cell anemia in 49 cases (34 males; 15 females) and Hb S-Î² thalassemia (S-Î²-thal) in 17 cases (nine males; eight females). There were also 46 cases (32 males; 14 females) of Î²-thal major, 103 cases (51 males; 52 females) of Î²-thal trait, six cases (four males; two females) of Hb E trait [Î²26(B8)Gluâ†'Lys; GAGâ†'AAG], and 17 cases (12 males; five females) of Hb E-Î²-thal (E-Î²-thal). A large proportion of these anomalies were found among the general caste people rather than among the tribal population which constitutes 22% of the total population in this state. Hb E was found mainly in higher castes like Khandayat and Karan,

residing in the coastal region of Orissa. This study provides comprehensive data on the spectrum of hemoglobinopathies in this state.

10. **Distinctive mutation spectrum of the HBB gene in an urban eastern Indian population**

    2014

    Hemoglobin

    Sahoo, S S and Biswal, S and Dixit, M

Hemoglobinopathies such as Î²-thalassemia (Î²-thal) and sickle cell anemia (or Hb S [Î²6(A3)Gluâ†'Val]) impose a major health burden in the Indian population. To determine the frequencies of the HBB gene mutations in eastern Indian populations and to compare with the available data, a comprehensive molecular analysis of the HBB gene was done in the normal Odisha State population. Using polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP), amplification refractory mutation system (ARMS) and DNA sequencing techniques, Î²-thal and sickle cell anemia mutations were characterized in 267 healthy individuals. Entire HBB gene sequencing showed 63 different mutations including 11 new ones. The predominant mutation HBB: c.9T,>,C was observed at a high frequency (19.57%) in the normal population. In the urban population of Odisha State, India, carrier frequency of hemoglobinopathies was found to be 18.48%, and for Î²-thal, the carrier rate was 14.13%, which is very high indeed. In the absence of a complete cure by any expensive treatment and drug administration, this information would be helpful for planning a population screening program and establishing prenatal diagnosis of Î²-thal in order to reduce the burden of such a genetic disease. Â© 2014 Informa Healthcare USA, Inc.

11. **The spectrum of haemoglobin variants in two scheduled tribes of Sundargarh district in north-western Orissa, India**

    2005

    Annals of Human Biology

    Balgir, R S

Background: Tribal communities in India constitute a major part of the population and are vulnerable to many erythrocytic hereditary and haematological disorders such as haemoglobinopathies. Genetic studies so far undertaken on tribal groups are scanty, patchy and incomplete. No field-based systematic studies of hereditary haemolytic disorders in Orissa are available. Further, the extent of haemoglobin variants among the tribals in the state is not known. The present study was carried out in the Bhuyan and Kharia tribes of Sundargarh district in Orissa. Aim: This study aims to find the prevalence/spectrum of haemoglobin variants in two major tribal groups, namely Bhuyan and Kharia and their subgroups, inhabiting the Sundargarh district in north-western Orissa. Subjects and methods: Following the probability proportionate to size cluster sampling procedure for villages, a randomized sampling procedure was adopted irrespective of the age, sex and individual susceptibility pattern, selecting exclusive villages of each sub-group of tribes in five blocks. A total of 1603 blood samples of 836 Bhuyan and 767 Kharia tribals were screened for haemoglobin variants in the Sundargarh district of Orissa. Laboratory analyses of blood samples were carried out following standard procedures. Results: The study showed a high prevalence of haemoglobin variants in the Bhuyan (9.8%) and Kharia (13.3%) tribes, sickle-cell disorders contributing 2.4% and 5.6%, respectively. The sickle-cell gene was found to be completely absent in the Dudh Kharia tribe, whereas the frequency in the Dhelki Kharia was quite high (12.5%). For the first time, 1.4% prevalence of haemoglobin E disorders (10 traits and one disease case) was recorded in a tribal population, i.e. Delki Kharia in Orissa. No other haemoglobin variant except Î²-thalassaemia trait was detected in the Dudh Kharia tribe (8.1%), showing their genetic isolation ($p < 0.001$) from the Delki Kharia (4.1%), the average being 6.3% in the Kharia tribe. Out of three subgroups of Bhuyan studied, the sickle-cell trait was detected only in Paraja (0.9%) and Paik (7.4%), and not in Paudi (Hill) Bhuyans. However, the Î²-thalassaemia trait was detected in an average 6.5% in the Bhuyan tribe: in Paudi (2.1%), Paik (7.8%) and in Paraja (12.7%). For the first time in the tribes of

Orissa a family was found with haemoglobin D trait (in Paik Bhuyan) and another with hereditary persistence of fetal haemoglobin (in Paraja Bhuyan). Clinical and haematological features of these disorders were similar to those reported in previous studies carried out in India. Conclusion: Isolates of the Bhuyan and Kharia tribes show intra-group variations in prevalence of haemoglobin variants due to founder effect, genetic drift, and the practice of inbreeding in varied geographical and ecological niches in the Sundargarh district of Orissa. Â© 2005 Taylor & Francis.

12. **Sickle cell gene in Central India: Kinship and geography.**

    1995

    American journal of human biology : the official journal of the Human Biology Council

    Das, M K

A wide range of variation (0.00-0.14) in the frequencies of the HbS allele has been observed among 16 tribes of Orissa, Madhya Pradesh, and Maharashtra. A significant excess of SS individuals over that expected under Hardy-Weinberg equilibrium was observed among 6 of 16 populations. These populations belong to three linguistic groups and have history of heterogeneous origins. A geographical cline of increase in HbS allele frequency from east to west is apparent. This pattern can largely be explained by differential migration. The kinship coefficient (r(ij)) and paired F(ST) do not show any significant correleation up to 250 km of geographical distance but beyond this distance they show an inverse releationship with increasing geographic distance. Hemoglobin levels between individuals with Î²(S) allele and with normal HbA individuals do not differ in these. Â© 1995 Wiley-Liss, Inc.

13. **Inadequate community knowledge about sickle cell disease among the Indian tribal population: a formative assessment in a multicentric intervention study.**

    2021

    Transactions of the Royal Society of Tropical Medicine and Hygiene

    Babu, Bontha V and Sridevi, Parikipandla and Surti, Shaily and Ranjit, Manoranjan and Bhat, Deepa and Sarmah, Jatin and Sudhakar, Godi and Sharma, Yogita

BACKGROUND: Sickle cell disease (SCD) is a serious public health problem, with >300 000 affected births worldwide each year. About 73% of the SCD-affected people in India belong to the tribal population. The Government of India is planning to implement a programme for SCD and hence people's knowledge of SCD is crucial. This paper reports the SCD-related knowledge among the Indian tribal population. METHODS: As part of a formative assessment before an intervention, data were collected from 9837 adults from 24 primary health centre areas of six states. Each community's knowledge of SCD was elicited through an interviewer-administered pretested questionnaire. Univariate and multivariate analyses were conducted. RESULTS: Overall, 32.1% (CI 31.2 to 33.1%) of participants had heard of SCD, 7.9% (CI: 7.3 to 8.4%) knew that SCD is hereditary, 19.4% (CI: 18.7 to 20.3%) knew that a blood test can diagnose SCD and 23.9% (CI: 23.1 to 24.8%) knew that SCD is treatable. Only 13.1% (CI: 12.4 to 13.8%) knew that SCD can be prevented. No more than 16% knew about any SCD symptoms. Multiple logistic regression revealed some predictors of basic knowledge (i.e. had heard of SCD). CONCLUSIONS: There is a gross inadequacy of knowledge about SCD in the Indian tribal population. This study warrants implementing a health education programme as a part of the SCD programme.

14. **Influence of Sickle Cell Gene on the Allelic Diversity at the msp-1 locus of Plasmodium falciparum in Adult Patients with Severe Malaria.**

    2015

    Mediterranean journal of hematology and infectious diseases

    Patel, Dilip Kumar and Mashon, Ranjeet Singh and Purohit, Prasanta and Meher, Satyabrata and Dehury, Snehadhini and Marndi, Chhatray and Das, Kishalaya and Kullu, Bipin Kishore and Patel, Siris and Das, Padmalaya

Although several studies have supported that sickle cell trait (HbAS) protects against falciparum malaria, the exact mechanism by which sickle gene confers protection is unclear. Further, there is no information on the influence of the sickle gene on the parasitic diversity of P. falciparum population in severe symptomatic malaria. This study was undertaken to assess the effect of the sickle gene on the parasite densities and diversities in hospitalized adult patients with severe falciparum malaria. The study was carried out in 166 adults hospitalized subjects with severe falciparum malaria at Sickle Cell Clinic and Molecular Biology Laboratory, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Odisha, India. They were divided into three groups on the basis of hemoglobin variants HbAA (n=104), HbAS (n=30) and HbSS (n=32). The msp-1 loci were genotyped using a PCR-based methodology. The parasite densities were significantly high in HbAA compared to HbAS and HbSS. The multiplicity of infection (MOI) and multi-clonality for msp-1 were significantly low in HbSS and HbAS compared to HbAA. The prevalence of K1 ($p<0$ .0001) and MAD20 ($p=0.0003$) alleles were significantly high in HbAA. The RO33 allele was detected at a higher frequency in HbSS and HbAS, compared to K1 and MAD20. Sickle gene was found to reduce both the parasite densities and diversity of P. falciparum in adults with severe malaria.

15. **Clinical profile of sickle cell disease in Orissa.**

    1997

    Indian journal of pediatrics

    Kar, B C and Devi, S

Children comprised 52% of patients with Sickle Cell Disease (SCD). Types of Sickle Cell Disease encountered were SS (92.7%). SB thalassaemia (6.7%) and SD disease (0.7%). The disease was widespread in almost all castes and communities in the society; largest number of patients (20%) belonging to scheduled castes and only 1.4% were from scheduled tribes. Maximum number of cases were in the age group 2-4 and 4-6 years, many of whom died around this age. Besides attacks of pain, jaundice and anemia, frequent attacks of fever with anemia or only anemia in childhood were a predominant presenting feature. Splenic sequestration was frequent (10.1%). The patients usually had a steady state hemoglobin level of 6-10 g/dl, with which they thrived well. Fetal hemoglobin was 5-30%. Blood transfusion was not a frequent requirement, but prophylactic long acting penicillin was helpful in preventing frequency of crisis.

16. **Knowledge, awareness, and attitude of premarital screening with special focus on sickle cell disease: a study from Odisha**

    2020

    Journal of Community Genetics

    Bindhani, B K and Devi, N K and Nayak, J K

Sickle cell disease (SCD) is a genetic disorder with an estimated 5200 live births each year indicating towards a major public health issue in India. Although SCD has been described in India in numerous ethnic groups, it is most prevalent in tribal community. Prevalence of sickle cell gene is 5 to 34% in tribal communities, who have a

high prevalence of socioeconomic disadvantage and are frequently medically underserved. The objective of the present study is to explore the knowledge, awareness, and attitude of premarital genetic counseling and screening for sickle cell hemoglobin among individuals of Koraput district. A cross-sectional study design was employed and a total of 152 individuals were recruited using multistage sampling technique, including 43 individuals with sickle cell hemoglobinopathy. Data was collected using a pre-tested, self-administered questionnaire and analyzed using SPSS-20. Though people are aware of SCD and SCT, majority believe that sickle cell carriers transmit the disease and they do not know that marriage between sickle cell carriers need to be avoided.

17. **Fetal outcome and childhood mortality in offspring of mothers with sickle cell trait and disease.**

    1997

    Indian journal of pediatrics

    Balgir, R S and Dash, B P and Das, R K

The sickle cell hemoglobinopathy is a major public health problem which causes high morbidity and mortality in India. Although the hematological and clinical profile of the patients is extensively studies. The reproductive outcome of mothers afflicted with sickle cell trait and disease is still unknown in India. In a retrospective study, we have examined the reproductive profile of 190 mothers afflicted with sickle cell, attending Medical Out-Patient Department at V.S.S. Medical College Hospital, Burla in Western Orissa, India during the year 1991-1992. Seventy-three mothers who were found normal after medical examination and were free from hemoglobinopathic disorders, anemia, jaundice, iron deficiency, etc. constituted the control group and 66 mothers with sickle cell trait and 51 with sickle cell disease formed the study group. The reproductive history was recorded for number of conceptions, fate of offspring, live birth, surviving children and childhood mortality. Hematological investigations and hemoglobin electrophoresis were done as per the standard procedure. There was no difference in mean number of livebirths per mother between controls and sickle cell trait mothers. But between the controls and sickle cell homozygotes ($p < 0.01$), and sickle cell trait and disease ($p < 0.01$) mothers, this mean number was significant. For abortions/miscarriages, the difference between controls and sickle cell homozygotes ($p < 0.001$), and sickle cell trait and disease ($p < 0.01$) mothers was highly significant. The number of stillbirths per mother in homozygous sickle cell mothers was higher ($p < 0.01$) as compared to controls. There were significantly higher childhood deaths in sickle cell trait ($p < 0.05$) and disease ($p < 0.05$) mothers than in the controls. It seems that the sickle cell heterozygote and hemoglobin E heterozygote mothers are genetically better fit than the sickle cell homozygotes. Further, the sickle cell disease is clinically severer than the hemoglobin E disease in India probably due to molecular diversity.

18. **Infant mortality and reproductive wastage associated with different genotypes of haemoglobinopathies in Orissa, India.**

    2007

    Annals of human biology

    Balgir, R S

BACKGROUND: Haemoglobinopathies, including sickle-cell disease and thalassaemia syndrome, are a group of blood diseases mostly confined to tropical and subtropical regions of the world. The spectrum of haemoglobin variants is a group of commonly encountered genetic conditions, with an average frequency of 19.32% in Orissa, varying from region to region and from community to community depending upon the type of mating practices. AIM: For the first time, the infant mortality rate (IMR), i.e. the number of deaths under 1 year of age (in a given year) per thousand live births in a particular area, was studied to find the cause of the high IMR and to relate it to different genotypes of haemoglobinopathies. RESULTS: IMR was found to be higher in couples with sickle-cell trait (75.9), beta-thalassaemia (184.2), and sickle cell/beta-thalassaemia (70.2) compared to normal couples (26.3). The reproductive wastage (abortions, stillbirths and neonatal deaths) and the number of deaths of offspring below 1 year of age (infant mortality) and below 10 years of age (childhood mortality) among affected couples in such

families were also statistically significantly higher compared to normal parents. CONCLUSIONS: The progeny of sickle-cell trait, beta-thalassaemia trait, and sickle cell/beta-thalassaemia couples contributes substantially to the high neonatal/IMR in the coastal state of Orissa in Central-Eastern India. This study has revealed that in comparison to normal couples, couples who were carriers of haemoglobinopathies had a greater reproductive wastage. Screening and genetic counselling could be an important factor in reducing IMR in rural India. The traits/carriers of haemoglobinopathies should, specifically, avoid marriages and mating for the better health of subsequent generations.

19. **The sickle cell gene is widespread in India.**

    1987

    Transactions of the Royal Society of Tropical Medicine and Hygiene

    Kar, B C and Devi, S and Dash, K C and Das, M

The sickle cell gene was first described in India in a tribal population in the south, leading to the belief that it was confined to tribal groups. The present study confirms that it is widespread in the state of Orissa and spreads throughout Hindu society, being more common in upper and scheduled castes than in tribal groups.

20. **Sickle cell disease in Orissa State, India**

    1986

    Lancet

    Kar, B C and Kulozik, A E and Sirr, S

A study of 131 patients with homozygous sickle cell (SS) disease in Orissa State, India, indicated that, compared with Jamaican patients, Indian patients have higher frequencies of alpha thalassaemia, higher fetal haemoglobin, total haemoglobin, and red cell counts, and lower mean cell volume, mean cell haemoglobin concentration, and reticulocyte counts. Indian patients have a greater frequency and later peak incidence of splenomegaly, and hypersplenism is common. Painful crises and dactylitis are not uncommon in Indian patients but chronic leg ulceration is rare. Homozygous sickle cell disease in Orissa is similar to that in the Eastern Province of Saudi Arabia and is very different from that in populations of West African origin.

21. **Sickle cell disease prevents diabetes mellitus occurrence: A hospital based cross-sectional study.**

    2019

    Journal of family medicine and primary care

    Prusty, Biswaranjan and Soren, Thakura and Choudhury, Anurag and Biswal, Reshma and Pradhan, Dillip K and Thatoi, Pravat K

BACKGROUND: Sickle cell disease is the commonest inherited hemoglobinopathy. There are few reports point towards decrease incidence of diabetes mellitus in sickle cell disease patients. MATERIALS AND METHODS: This cross-sectional study was conducted in VIMSAR, Burla, Odisha between Nov 2014 to Oct 2016. FBS and 2 hours OGTT reports of adult sickle cell disease patients were compared with the same reports from equal no of adult persons without sickle cell disease (controls) to found out any significant difference in prevalence of diabetes mellitus in sickle cell disease patients versus controls. RESULTS: A total of 137 adult patients of sickle cell disease out of which males were 94 (68.61%) and females were 43 (31.38%) with an average age of (26.7 Â± 10.9) years and an equal number of controls [males 87 (63.8%) and females 50 (36.5%)] with an average age of (47.6 Â± 13.6) years were included in the study. We found diabetes mellitus in 2 (1.46%) out of 137 sickle cell disease patients with an average BMI 18.5 kg/m(2) versus 12 (8.76%) in equal number of controls with an average

BMI of 22.6 kg/m(2). CONCLUSION: This study concludes that prevalence of diabetes mellitus in sickle cell disease patients is significantly lower than non-sickle cell disease persons. This may be due to less longevity and low BMI in sickle cell disease patients.

22. Procalcitonin as a biomarker of bacterial infection in sickle cell vaso-occlusive crisis

2014

Mediterranean Journal of Hematology and Infectious Diseases

Patel, D K and Mohapatra, M K and Thomas, A G and Patel, S and Purohit, P

Sickle cell anaemia (SCA) patients with vaso-occlusive crisis (VOC) have signs of inflammation and it is often difficult to diagnose a bacterial infection in them. This study was undertaken to evaluate the role of serum procalcitonin (PCT) as a biomarker of bacterial infection in acute sickle cell vaso-occlusive crisis. Hundred homozygous SCA patients were studied at Sickle Cell Clinic and Molecular Biology Laboratory, V.S.S. Medical College, Burla, Odisha, India. All the patients were divided into three categories namely category-A (VOC/ACS with SIRS but without evidence of bacterial infection - 66 patients), category-B (VOC/ACS with SIRS and either proven or suspected bacterial infection - 24 patients) and category-C (SCA patients in steady state without VOC/ACS or SIRS - 10 patients). Complete blood count, C-reactive protein (CRP) estimation and PCT measurement were done in all the patients. There was no significant difference in TLC and CRP values between category-A and B. In category-A, the PCT level was <0.5 ng/mL in 83.3% and 0.5-2 ng/mL in 16.7% of cases. In category-B, all the patients had PCT value >0.5 ng/mL with 87.5% of patients having >2 ng/mL. In category-C, PCT value was <0.5 ng/mL. PCT had a high sensitivity (100%) and negative predictive value (100%) for bacterial infection at a cut-offvalue of 0.5 ng/mL; whereas the specificity is excellent at a cut-offvalue of 2 ng/mL. SCA patients with VOC/ACS and SIRS having a PCT level of <0.5 ng/mL have a low probability of bacterial infection whereas PCT value of >2 ng/mL is indicative of bacterial infection necessitating early antimicrobial therapy.

23. Spectrum of hemoglobin disorders in southern Odisha, India: a hospital based study.

2021

Porto biomedical journal

Sahu, Pramita and Purohit, Prasanta and Mantri, Santwana and Tudu, Ramray and Nayak, Jayanti and Agrawalla, Sunil Kumar and Behera, Samira Kumar and Patro, Manoj Kumar and Karmee, Nivedita and Tripathy, Diptimayee and Mishra, Bharati and Mishra, Debi Prasad

BACKGROUND: Hemoglobin disorders are the leading health concern in the world including India. There is a paucity of literature on the spectrum of hemoglobin disorders in southern districts of Odisha state. This study was undertaken to elucidate the occurrence of different hemoglobin disorders in a tertiary health care facility of Odisha state, India. METHODS: The study cases were suspected patients of all age groups advised for screening of different hemoglobin disorders. Hemoglobin disorders were screened by sickling slide test and high-performance liquid chromatography (HPLC) using the Variant-II hemoglobin testing system as per the manufacturer's guidelines. RESULTS: Over 2 years, 2332 blood samples (including 1102 pediatric and 1230 adult cases) were investigated, out of which, 1380 (59.2%) of cases had abnormal hemoglobin disorders. The most common was sickle cell disorders (48.67%, 1135/2332) followed by Î²-thalassemia (11.32%, 264/2332). Some rare variants were detected as hemoglobin D(-Punjab), hemoglobin E, hemoglobin Lepore, hereditary persistence of fetal hemoglobin, hemoglobin with high P2 window, hemoglobin with high P3 window etc, Among the cases with abnormal hemoglobin disorders, 744 (53.9%), 545 (39.5%) and, 91 (6.6%) cases were found to have the heterozygous, homozygous and, double heterozygous state. Of the 188 ante-natal cases screened, 31.4% of cases had abnormal hemoglobin variants with sickle cell disorders being the most prevalent one. CONCLUSION: Along with the high occurrence of sickle cell disorders in the study area, some other rare hemoglobin disorders are also prevalent which calls for a large community-based cohort study.

24. **Prediction of outcome of severe falciparum malaria in Koraput, Odisha, India: A hospital-based study.**

    2014

    Tropical parasitology

    Das, Lalit Kumar and Padhi, Bishwanath and Sahu, Sudhansu Sekar

BACKGROUND AND OBJECTIVES: Infection with Plasmodium falciparum, caused 627,000 deaths in 2012 in the world. P. falciparum infection causes myriads of clinical manifestations. Exact clinical manifestation resulting in poor prognosis in hyper-endemic epidemiological settings need to be ascertained to save human lives. A hospital-based study was conducted to elucidate the different severe clinical presentations of falciparum malaria and to examine the critical clinical and laboratory parameters on the prognosis of these severe manifestations in a stable hyper-endemic falciparum area in the state of Odisha, India. MATERIALS AND METHODS: Consecutive patients admitted in a tertiary care hospital with severe manifestations of malaria as per WHO criteria and confirmed by parasitological examination were included in the study. A detailed clinical and biochemical parameters were examined. Clinical data were reviewed before being double entered into a computer and analyzed. Statistical analyses were carried out using Epi Info 6.04. Continuous and normal distributed data were compared by two-tailed Student's t-test and proportions compared with Ï‡(2) tests with Yates' correction or Fisher's exact test. RESULTS AND DISCUSSION: A total of 1320 patients with clinical malaria, diagnosed at outpatients' department were admitted in the hospital during the 1 year study period of which, 292 (22.1%) were children under 14 years of age. The major clinical categories on admission were hyperpyrexia (70.7%), cerebral malaria (9.4%), malarial anemia (7.7%), algid malaria (1.5%), and malaria associated categories were respiratory infection (2.2%), hepatitis (2.0%), urinary tract infection (1.8%), enteric fever (3.3%), and sickle cell disease (1.2%). The overall case fatality rate (CFR) was 4.3 (57/1320). The CFR in children 12.3 (36/292) was significantly higher when compared to adults, that is, 2.0 (21/1028). The major causes of death were cerebral malaria (45.6%), malaria along with a respiratory infection (19.3%) and anemia (10.5%). Malarial anemia along sickle cell disease accounted for 19.3% of all malaria related deaths. Proportion of mortality due to acute renal failure was higher in adults. Biochemical parameters suggest involvement of multiple organs. The findings suggest that the area can be effectively managed by sustained and continuous preventive and curative efforts.

25. **Do tribal communities show an inverse relationship between sickle cell disorders and glucose-6-phosphate dehydrogenase deficiency in malaria endemic areas of Central-Eastern India?**

    2006

    HOMO- Journal of Comparative Human Biology

    Balgir, R S

Tribal communities in India constitute the largest tribal population in the world. There are about 635 biological isolates (tribes and subtribes), which constituted 8.08% (about 84.3 million) of the total population of India as per the 2001 census. Out of 635 scheduled tribes (aborigines), 62 live in the state of Orissa alone forming about 10.8% of the tribal population of India. Orissa state occupies an important place, being the 3rd in rank for the highest concentration of tribal population in the country. In India, tribal communities are highly vulnerable to hereditary diseases and have a high degree of malnutrition, morbidity and mortality. The sickle cell haemoglobinopathy and glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency are important genetic and public health problems in Central-Eastern part of India. In order to map out these genetic disorders among the tribal people, a cross-section of 15 major tribal communities from different parts of Orissa was randomly screened for haemoglobin variants and G6PD deficiency. The high frequency of sickle cell haemoglobinopathy (0-22.4%) and G6PD deficiency (4.3-17.4%), with Î²-thalassemia trait (0-8.5%) taking almost an intermediate position, was observed. For G6PD deficiency, hemizygous males as well as female heterozygotes and female homozygotes were detected.

Twelve cases showed compound heterozygosity for sickle cell haemoglobinopathy and G6PD deficiency. There seems to be a trend towards an inverse relationship between the sickle cell allele and G6PD deficiency, and sickle cell and Î²-thalassemia allele in a cross-section of malaria endemic (Plasmodium falciparum) tribal communities in Orissa. When the frequency of sickle cell allele decreases in a cross-section of malaria endemic tribal population, the frequency of G6PD enzyme deficiency and Î²-thalassemia allele increases and vice versa. Natural selection had played a major role in favour of sickle cell, Î²-thalassemia and G6PD mutation alleles so that they had probably evolved as a protective mechanism against the lethal effects of malaria in this part of the country. However, the calculated values of 0.074, 0.218 and 0.337, respectively, of Pearson's correlation co-efficient (r), showed no correlation between sickle cell disorders and G6PD deficiency, sickle cell disorders and Î²-thalassemia, and G6PD deficiency and Î²-thalassemia. Â© 2006 Elsevier GmbH. All rights reserved.

26. Profile of hemoglobinopathies in the state of Odisha

2012

Indian Journal of Hematology and Blood Transfusion

Lenka, A and Sethy, S and Nayak, R and Jena, R K and Mohanty, P

Objectives: To determine the clinical and hematological profile of different hemoglobinopathies. Materials and Methods: Patients with clinical features of chronic hemolytic anemia without history of blood transfusion in last three months attending the department of clinical hematology of SCB Medical College & Hospital, Cuttack from November 2007 to February 2012 are included in the study. About 2 ml of blood was collected from each patient which was investigated in fully automated capillary zone electrophoresis. Screening tests like sickling test and complete blood count by five part cell counter (sysmax 2000I) were done in all cases. Results: Out of total 6,195 cases hemoglobinopathy was found in 3,263 cases. Beta-thalassemia constitutes 28.1 % cases with 21.02 %of trait, 4.51 %thalassemia intermedia and 2.57 % of thalassemia major cases. Sickle cell disorder was found in 27.03 % cases with sickle cell trait in 23.17 % and sickle cell disease in 3.86 % cases. Sicke-beta thal was 21.88 %.Hb Ewas found in 2.69 %cases and E-beta thal in 9.65 % cases. Conclusion: Hemoglobinopathy is common in almost all parts of Odisha. They cause high degree of morbidity and mortality along with socio- economic burden. In this study diagnosis could not be confirmed in 8.8 % of cases which needs further investigations like parental evaluation and globin chain mutation analysis.

27. Haemoglobinopathies in Odisha: Six years experience of the Odisha sickle cell project (NHM), Vimsar, Burla, Odisha, India

2017

International Journal of Laboratory Hematology

Meher, S and Mohanty, P K and Das, K and Patel, S and Sarkar, B and Dehury, S and Sahoo, S

Introduction: Hemoglobinopathies is a serious health problem in Odisha with significant morbidity and mortality. Sickle cell haemoglobinopathies is much more diversity in country like India with a multi ethnic mosaic. In this communication we report the spectrum of haemoglobinopathies and thalassaemias in Odisha as documented by the Odisha Sickle Cell Project (OSCP) in over six years. The findings are imperative in understanding the epidemiology of sickling and non sickling haemoglobinopathies in Odisha. Methods: A total of 62698 individuals were screened between April 2010 to December 2016 by sickling test, alkaline agarose-gel haemoglobin electrophoresis, CE-HPLC (Bio-Rad, Variant-II) and molecular methods (PCR-ARMS, RE-PCR, GAP-PCR, HBB sequencing). We have detected compound heterozygotes involving HbS allele in 605 patients and non-sickling haemoglobinopathies (NSH) in 396 individuals. Results: Homozygote HbS the most common genotype along with nine states of compound heterozygosity were confirmed causing sickle cell haemoglobinopathy in Odisha (with b-thalassaemia, HbD, HbE, HbC, HbHofu, HbTianshui, HbLepore, HbQIndia and db-thalassemia).

Nineteen NSH were caused by 8 rare variants (HbD, HbE, HbHofu, HbLimassol, HbLepore, HbQIndia, HbDIran & HbH) and thalassaemias with various allelic combinations. We confirmed 15 cases of Indian deletion inversion Gg(Agdb)0-thalassemia and HPFH-3 in several combinations. In addition, 3 rare b0-thalassaemia mutations (Cd15(-T), Cd16(-C), 17bp del)were also confirmed in our patients. Conclusions: In past 80 months, 28 variable phenotypes were confirmed in 1001 individuals. The findings portrayed in this communication indicate high allelic diversity of haemoglobinopathies in Odisha, many of which hitherto are not reported from India. Research outcomes of progressive OSCP with respect to the variation of haemoglobinopathies in the state are remarkable. Our findings of uncommon b0-thalassaemia mutations and several rare variants strengthens the haemoglobinopathy database of the state.

28. Profile of haemoglobinopathies in Odisha: A 5-year institutional study

2014

Indian Journal of Hematology and Blood Transfusion

Sahoo, S S and Jena, R K and Mohanty, P and Das, B P

Introduction: Thalassemias and other haemoglobinopathies are highly prevalent in Odisha & other states of eastern India. Accurate and precise separation of haemoglobin types, together with reliable quantitation, are essential for differential diagnosis and effective management of these diseases. Objectives: To study the pattern of Hemoglobinopathy in Odisha-a tertiary centre study of 5 years duration. Materials and Methods: Patients showing features of Haemolytic anaemia in Peripheral Smear (both children and adults) were evaluated with automated capillary zone electrophoresis (Minicap Sebia): 2 ml of EDTA blood after centrifugation & discarding the supernatant was used; Effective quality control was maintained. Results: Total number of cases-5,671. Number of cases with normal study-2,458. A normal haemoglobin cases-3,213. Beta-thal(trait)- 628(19.54 %); beta-thal(homozygous)-473(14.72 %); SCD(trait)- 762(23.72 %); SCD(homozygous)-462(14.38 %). Sickle beta-thalassemia- 533(16.59 %); HbE beta-thalassemia-57(1.77 %); HbE (disease)-175 (5.45 %); HbE(trait)-98(3.05 %) alpha-thalassemia- 25 (0.78 %). Conclusion: Highest no. of cases of Sickle cell trait followed by beta-thalassemia trait. Lowest no. of cases of alpha-thalassemia followed by HbE thalassemia. High prevalence of cases of sickle cell with co-existent beta-thalassemia. Traits more common than homozygous variants except in cases of HbE disease. Abnormal Haemoglobin patterns-SCD(trait) >beta-thalassemia(trait) >Sickle beta-thalassemia> beta-thalassemia(homozygous) >SCD(homozygous) >HbE(disease) > HbE(trait) >HbE thalassemia>alpha-thalassemia.

29. Study on ocular manifestations of sickle haemoglobinopathies.

1985

Indian journal of ophthalmology

Das, G and Behera, U C and Kar, B C

30. Spectrum of Hemoglobinopathies Among the Primitive Tribes: A Multicentric Study in India.

2015

Asia-Pacific Journal of Public Health

Mohanty, Dipika and Mukherjee, Malay B and Colah, Roshan B and Wadia, Mahrukh and Ghosh, Kanjaksha and Chottray, Guru Prasad and Jain, Dipty and Italia, Yazdi and Ashokan, Kumar S and Kaul, Rajni and Shukla, Deepak K and Muthuswamy, Vasantha

SCREENING AND DIAGNOSIS

1. **Genetic heterogeneity of population structure in 15 major scheduled tribes in central-eastern India: A study of immuno-hematological disorders**

   2006

   Indian Journal of Human Genetics

   Balgir, R S

Background: The aboriginal tribes of India constitute an important segment of the society in the world. Though a large number of genetic studies have been carried out in India, the genetic data of the populations in the state of Orissa are very limited, especially pertaining to the indigenous tribal people. Most of the earlier studies were restricted to either a single tribe or a few genetic markers. Data on population structure of tribal communities of Orissa pertaining to common hemolytic disorders and genetic variations are still scanty. AIMS AND OBJECTIVES: In view of the limited data available on the tribes and the huge tribal population, a cross-section of ashram schools was investigated for immuno-hematological disorders in relation to geographical, linguistic and genetic variations. MATERIALS AND METHODS: A cross-section of 15 major scheduled tribes in ashram schools from eight districts of Orissa was randomly studied for five hereditary immuno-hematological markers, namely, the ABO and Rhesus (D) blood groups, sickle cell hemoglobinopathy, Î²-thalassemia syndrome and G-6-PD deficiency, following the standard hematological procedures and techniques. RESULTS: A preponderance of blood group B over A and low incidence of Rhesus-negative (D-) among Bathudi, Bhuyan, Kissan, Kolha, Kondh, Munda oraon, Paraja, Santal and Saora tribes was observed. The deficiency of G-6-PD enzyme was found to be quite high, varying from 5.1 to 15.9% among these scheduled tribes of Orissa. Both deficient female heterozygotes and homozygotes were encountered. Marked variation was seen in the prevalence of Î²-thalassemia trait, varying from 0 to 8.5%, in the aboriginal tribes. The frequency of sickle cell disorders was found to vary from 0 to 22.4% among the major tribes, but it was comparatively higher in Paraja (21.5%), Dhelki Kharia (13.7%), Gond (11.9%) and Bhatra (10.5%) tribes. CONCLUSIONS: The study showed genetic heterogeneity and diversity with respect to above immuno-hematological genetic markers and indicated not only the inter-tribal admixture but also diffusion with other racial groups of India. Further, the heterogeneous tribal populations from Orissa were found to harbor almost all major hemoglobinopathies. This is the first comprehensive study of immuno-hematological disorders among the scheduled tribes from the state of Orissa.

2. **Haemoglobin E/Î²-thalassaemia - An experience in the eastern indian state of orissa**

   2003

   Acta Haematologica

   Chhotray, G P and Dash, B P and Ranjit, M R and Cohla, R B and Mohanty, D

3. **Genotype-phenotype correlation of Î²-thalassemia spectrum of mutations in an Indian population**

   2012

   Hematology Reports

   Sahu, Praveen Kishore and Pati, Sudhanshu Shekhar and Mishra, Saroj Kanti

Coexistence of thalassemia, hemoglobinopathies and malaria has interested geneticists over many decades. The present study represents such a population from the eastern Indian state of Orissa. Children and their

siblings (n=38) were genotyped for Î²-thalassemia mutations and genotype-phenotype correlation was determined. The major genotype was IVS 1.5 mutation: 26% homozygous (n=10) and 37% (n=14) double heterozygous with other mutations or hemoglobinopathies. Sickle hemoglobin was the major associated hemoglobinopathy (n=12, 32%). Other mutations found were Cd 8/9, HbE and Cd 41/42. The study population did not contain any IVS 1.1 mutations which is the second major Indo- Asian genotype. Genotype-phenotype correlation revealed that genotypes of IVS 1.5, Cd 8/9 Cd 41/42 alone or in association, exhibit severe, moderate and mild severity of thalassemia, respectively. Identification of the mutation at an early age as a part of new born screening and early intervention may help reduce the thalassemia-related morbidity.

4. **Clinical impact of factor V Leiden, prothrombin G20210A, and MTHFR C677T mutations among sickle cell disease patients of Central India**

   2013

   European Journal of Haematology

   Nishank, S S and Singh, M.P.S.S. and Yadav, R

Background: It is known that patients with sickle cell disease (SCD) present activation of the blood coagulation and fibrinolytic systems, especially during vaso-occlusive crises and also during the steady state of the disease. We determined whether the presence of the factor prothrombin gene G20210A variant, factor V gene G1691A mutation (factor V Leiden), and methylenetetrahydrofolate reductase (MTHFR) C677T polymorphisms may be risk factors for vascular complications in individuals with SCD. Methods: The study involved 150 patients with sickle cell anemia and 150 healthy controls of Central India. Genotyping of three thrombophilic mutations was carried out by PCR-RFLP methods using MnlI, Hind III, and Hinf I, respectively, for factor V Leiden, prothrombin, and MTHFR mutations. Results: Patients with SCD had significantly higher prevalence of mutant variants of MTHFR gene (28.0% heterozygotes and 14.6% homozygotes) and FVL gene (14.6% heterozygotes) as compared to normal/control individuals, but complete absence of mutant variants of prothrombin gene. The patients with SCD having mutant variants of MTHFR and FVL genes showed higher incidence of pain in chest, abdomen, and bone joints along with early age of onset of clinical manifestations as well as frequent dependence on blood transfusion than those patients with SCD having wild variants of these thrombotic genes. As compared to control subjects, SCD individuals having mutant variants of FVL and MTHFR genes had significant association with higher levels of prothrombin fragment (F1+2), D-dimer, thrombin-antithrombin (TAT), and lower level of protein C. Conclusion: MTHFR C677T and FVL G1691A polymorphisms may be risk factors for increased vascular complications in patient with SCD. Â© 2013 John Wiley & Sons A/S.

5. **Genetic diversity of hemoglobinopathies, G6PD deficiency, and ABO and Rhesus blood groups in two isolates of a primitive Kharia Tribe in Sundargarh District of Northwestern Orissa, India**

   2010

   Journal of Community Genetics

   Balgir, R S

Tribal communities constitute about 8.2% of the total population of India. Their health needs are even larger than elsewhere in India; this study investigates the genetic diversity in relation to hemoglobinopathies, G6PD deficiency and, ABO and Rhesus (D) blood groups in twosects, i.e. Dudh (converted Christian) and Dhelki(Hinduised) Kharia, a primitive tribe in Sundargarh district of Orissa in Central-Eastern India. A randomized screeningof 767 Kharia tribals (377 males and 390 females) belonging to all age groups and both sexes was done.Laboratory analysis was carried out following the standardmethodology and techniques. Contrasting differences were observed in the frequency of hematological genetic disorderssuch as Î²-thalassemia, sickle cell, hemoglobin E,G6PD deficiency, ABO and Rhesus (D) blood groups between the two subgroups. Dudh Kharia had no hemoglobin variant allele other than the high prevalence of Î²-thalassemia trait (8.1%), whereas, their counterpart Dhelki Kharia had the high prevalence of sickle cell allele (12.4%), hemoglobin E allele (3.2%),

and Î²-thalassemia allele (4.0%). Frequency distribution of hemoglobin variants between Dudh and Dhelki Kharia tribe was statistically highly significant (p<0.001). High G6PD deficiency was detected 19.2% and 30.7% in Dudh Kharia and Dhelki Kharia, respectively (p<0.001), the average being 24.4% in Kharia tribe. Kharia tribes show a trend for replacement of sickle cell gene with G6PD-deficiency gene as the clinical manifestations of G6PD deficiency are mild (do not result in a complete loss of enzyme activity) against the sickle cell disease with high morbidity and mortality. Rhesus (D)-negative blood group was 1.1% in Dudh Kharia and absent in Dhelki Kharia (p<0.05). This study showed genetic isolation of the two sects of Kharia tribe. Antimalarial drugs administration needs to be done with caution. Hematological disorders pose a major health challenge having multifaceted implications in public health genetics. Â© Springer-Verlag 2010.

6. Clinical and molecular characterization of Hb Hofu in eastern India

2014

International Journal of Laboratory Hematology

Purohit, P and Mashon, R S and Patel, S and Dehury, S and Pattanayak, C and Das, K and Nair, S and Italia, K and Bag, S and Colah, R and Patel, D K

Introduction: Hb Hofu (HBB:c. 380T>A) is a rare inherited hemoglobin abnormality with few case reports in the world literature. Methods: Screening for the sickle cell gene mutation and other hemoglobinopathies was carried out using the sickle slide test, Hb electrophoresis, and HPLC under an ongoing central government project. Results: We detected twelve Hb Hofu heterozygotes and three sickle Hb Hofu compound heterozygotes. The heterozygotes were asymptomatic except for one individual who had chronic kidney disease and moderate anemia. Only one HbS-Hofu case was symptomatic and presented with intermittent attacks of painful crisis. In the carrier state, the Hb Hofu eluted as a hump at the beginning of the HbA0 window. But in HbS-Hofu cases, Hb Hofu eluted as a single peak in the HbA0 window, with the HbA2 levels being >4% consistently. Conclusion: HbS-Hofu has a variable clinical presentation. The retention time of Hb Hofu on HPLC is very close to that of HbA0 and often elutes in the A0 window. Thus, there is every possibility of the HbS-Hofu chromatogram to be misinterpreted as that of a sickle cell trait/transfused sickle cell-beta-thalassemia case. This is the first time where Hb Hofu has been detected by HPLC, which is the widely accepted screening technique for hemoglobinopathies around the world. Â© 2013 John Wiley & Sons Ltd.

7. The 'odisha sickle cell project'-a new horizon of hope for sickle cell aggrieved patients in Odisha

2012

Indian Journal of Hematology and Blood Transfusion

Patel, S and Patel, D K and Purohit, P and Dehury, S and Bishwal, S C and Meher, S and Pradhan, B and Das, K

Introduction: Sickle cell disease (SCD) is a serious health problem in Odisha with significant morbidity and mortality. It is a huge burden for the patients and his families and a serious challenge to the medical fraternity. However the major constraint for management of this problem is non-availability of health facility in remote areas and lack of awareness amongst health care professionals about the various treatment of this disease. In view of this, National Rural Health Mission (NRHM), Govt. of Odisha sponsored Odisha Sickle Cell Project. Objective: Screening of population for sickle cell haemoglobinopathies and develop an infrastructure for investigation, registration, treatment, follow-up and counselling of all patients with SCD of Odisha. Materials and Method: The Odisha Sickle cell Project (OSCP) was started in April-2010, under this project Sickle cell unit were constructed at six DHHs of Western Odisha. Counselling and diagnosis of sickle cell patients at peripheral hospitals is done by a field worker and trained Laboratory technician. A state-of-art Molecular Biology & Haematology Laboratory has been developed at the referral centre, V.S.S. Medical College & Hospital, B urla. Cases referred from periphery are examined, counselled, registered here. This laboratory has facility for Hb electrophoresis, CBC,

Biochemical test, CE-HPLC, PCR & Flow Cytometry on a routine basis. Severe cases of SCD are started Hydroxyurea therapy at a low dose (10 mg/kg body wt/day). 2073 individuals have been screened for sickle cell haemoglobinopathies in 14 health camps organised in various districts of western Odisha. Simultaneously 10 CMEs have been coordinated for creating awareness among the doctors. Results: Till date the number of patients examined, counselled, diagnosed to have sickle cell haemoglobinopathies at VSS Medical College & Hospital, Burla are 28321, 13720 and (Table Presented) 5840 respectively. At six DHHs the number of new cases of sickle cell haemoglobinopathies detected are 1381, 737, 568, 1005, 578 and 1020 at Bolangir, Bargarh, Sambalpur, Jharsuguda, Deogarh and Sundergarh, respectively. Of the 5840 cases registered 5335 HbSS, 194 HbS-Î² thalassemia, 36 HbSD, 56 HbAD, 13 HbSE, 18 HbAE, 2 HbSC, 16 Î²thalassemia major, 160 Î² thalassemia trait, 5 GÎ³(AÎ³Î´Î²)0 thalassemia and 5 HPFH. 1997 no. of cases has been started Hydroxyurea (10 mg/kg body wt/day). It has been observed that low dose Hydroxyurea is effectively reducing the frequency of VOC and blood transfusion. Conclusion: Under OSCP we have diagnosed thousands of new cases of Sickle cell haemoglobinopathies, counselled them and have created awareness among the doctors of Western Odisha for better management and treatment of this Sickle Cell Disease.

8. **G452(P) 'Counting the uncounted': a descriptive study of the diagnoses presenting to a community paediatric clinic in odisha state, india**

   2020

   Archives of Disease in Childhood

   Nye, A and Cusack, M and Marelli, P and Norris, E and Morris, C

Introduction Odisha State had the third worst health index ranking among Indian states in 2017â€“2018. Relative to India as a whole, it has significantly worse infant mortality rate, under 5 mortality rate, and vaccination coverage. Although free public healthcare should be provided for those living below the poverty line, poor and vulnerable children are often denied medical treatment due to institutional bias.Our charity provides free healthcare, childcare and education for poor and underprivileged children. The clinic provides primary health care for children enrolled in the charityâ€™s school and preschools; and Paediatric care for children with disabilities or chronic disease. A disproportionately high number have significant medical conditions, as they are unable to access quality health care via conventional means.AimsTo describe the epidemiology of our patients and the range of conditions seen.MethodsThe notes of all Paediatric patients who attended the clinic from September 2018 to August 2019 were reviewed.ResultsOver the year, there were 1008 patient encounters. 57% were by males. The age range was from 1 month to 15 years (median 6 years). 63% of encounters were for management of acute illness, 11% were due to trauma, and 23% were related to chronic disease management. The most common diagnoses were lower respiratory tract infection, viral upper respiratory tract infection, tonsillitis, gastroenteritis and dental problems. Of the acute infections, it was presumed that 49% were bacterial, 39% viral, 9% parasitic and 5% fungal. â€˜Tropicalâ€™ infections encountered include typhoid, TB, dengue fever and HIV. Of the patient encounters that related to chronic diseases, the most common underlying diagnosis was cerebral palsy. Other significant long-term conditions include: sickle cell disease, thalassaemia, spina bifida, hydrocephalus, congenital heart disease, diabetes mellitus and hepatocellular carcinoma.ConclusionWithout this clinic, many of the children would have been unable to access healthcare, and may have experienced increased long-term morbidity or mortality. Children, including those with disabilities, are now able to access appropriate and prompt management of acute and chronic illness. We have demonstrated the impact a low-resource clinic can have, and hope to replicate this model across the state.

TREATMENT

1. **The effect of hydroxyurea on compound heterozygotes for sickle cell-hemoglobin D-Punjab-A single centre experience in eastern India.**

   2014

   Pediatric Blood & Cancer

   Patel S, Purohit P Mashon R S Dehury S Meher S Sahoo S Dash S S Das K Das P and Patel, Dilip Kumar and Patel, Siris and Purohit, Prasanta and Mashon, Ranjeet Singh and Dehury, Snehadhini and Meher, Satyabrata and Sahoo, Sulia and Dash, Subhransu Sekhar and Das, Kishalaya and Das, Padmalaya and Patel, Dilip Kumar

BACKGROUND: Although hydroxyurea is the only effective agent for the treatment of sickle cell disease, published experience with this drug is limited to treatment of homozygous sickle cell anemia and HbS/[beta] thalassemia. The role of hydroxyurea in the treatment of patients with HbSD-Punjab, a rare hemoglobinopathy with phenotypic expression similar to that of sickle cell anemia is unknown. PROCEDURE: Over a period of 10 years, we followed 42 patients with HbSD-Punjab, of which 20 presented with severe clinical manifestations (>=3 episodes of VOC and/or >=2 units of blood transfusion in the previous 12 months). These 20 patients were enrolled for treatment with hydroxyurea at a dose of 10 mg/kg/day and followed prospectively for a period of 24 months. RESULTS: The frequency of VOC decreased significantly and none of them required blood transfusion while receiving hydroxyurea. The HbF, total hemoglobin, MCV, MCH, and MCHC levels increased significantly, whereas HbS, WBC, platelet count, total serum bilirubin, and LDH levels decreased significantly in all the patients. No short-term drug toxicity was observed. CONCLUSION: This study describes the use of hydroxyurea therapy in patients with HbSD-Punjab. Low dose hydroxyurea (10 mg/kg/day) was found to be effective in reducing the clinical severity in patients with HbSD-Punjab without any short-term toxicity. In view of easy affordability amongst poor patients, widespread acceptability by patients and doctors, the need of infrequent monitoring and its potential effectiveness, low dose hydroxyurea is suitable for treatment of patients with HbSD-Punjab. Pediatr Blood Cancer 2014; 61:1341-1346. Â© 2014 Wiley Periodicals, Inc.

2. **Intravenous Acetaminophen vs Intravenous Diclofenac Sodium in Management of Skeletal Vaso-occlusive Crisis Among Children with Homozygous Sickle Cell Disease: A Randomized Controlled Trial**

   2021

   Indian Pediatrics

   Panda, P C and Mishra, N R and Patra, C S and Nayak, B K and Panda, S K

Objective: To compare the efficacy of intravenous acetaminophen and intravenous diclofenac sodium in the management of skeletal vaso-occlusive crisis among children with sickle cell disease. Design: Single blind randomized controlled trial. Setting: Tertiary care hospital. Participants: 104 children with sickle cell disease and skeletal vaso-occlusive crisis. Intervention: Intravenous acetaminophen at 10mg/kg/dose 8 hourly and intravenous diclofenac sodium at 1mg/kg/dose 8 hourly in 1:1 ratio. Main outcome measures: Reduction in pain score (50%), number of doses needed to relieve pain after 24 hours of drug administration and decrease in pain score at 1 hour. Results: A 50% reduction in pain score was seen in 35 (77.3%) and 10 (21.7%) children among acetaminophen and diclofenac sodium groups respectively (RR, 95% CI 3.6; 2.02â€“6.33, P< 0.001). The mean (SD) fall in pain score at 1 hour was significantly higher among intervention arm as compared to control arm [1.51 (0.5) and 1.06 (0.5); P<0.001]. Eight (17.4%) patients developed local phlebitis at the site of infusion among diclofenac group.

Conclusion: Intravenous acetaminophen is a better alternative to intravenous diclofenac in children with skeletal vaso-occlusive crisis.

3. **Study of Seminal Fluid Parameters and Fertility of Male Sickle Cell Disease Patients and Potential Impact of Hydroxyurea Treatment**

   2017

   The Journal of the Association of Physicians of India

   Sahoo, L K and Kullu, B K and Patel, S and Patel, N K and Rout, P and Purohit, P and Meher, S

INTRODUCTION: Male Sickle cell disease (SCD) patients often have moderate to severe hypogonadism resulting in abnormal seminal fluid parameters due to testicular dysfunction. Hydroxyurea (HU), the only drug found to be effective in preventing morbidity and mortality in sickle cell disease patients has been found to further aggravate the testicular dysfunction. MATERIAL AND METHODS: This was a prospective study done at a tertiary care hospital over 26 months between September 2011 to October 2013. 100 male sickle cell disease patients of age group 15 to 45 years were recruited in the study. We evaluated seminal fluid indices in all patients and the effect of hydroxyurea on seminal fluid parameters. Hydroxyurea was given at low dose of 10mg/kg/day orally to patients with frequent vaso-occlusive crisis and frequent need of blood transfusion. Seminal fluid analysis was done according to WHO criteria before starting hydroxyurea and every 3 months after initiation of hydroxyurea. Patients with abnormal seminal parameters before hydroxyurea therapy were not given hydroxyurea therapy. Patients with abnormal sperm parameters were subjected for FNAC of testis. In sickle cell disease patients with hydroxyurea therapy, who developed abnormal seminal fluid parameters, hydroxyurea was stopped for 3 months and seminal fluid parameters were re-evaluated. Patients who had recovery of seminal indices after hydroxyurea cessation were restarted with hydroxyurea therapy at low dose. RESULTS: Among Sickle cell disease patients without hydroxyurea therapy, 18% of patients developed oligospermia and 4% developed azoospermia. Among sickle cell disease patients with hydroxyurea therapy, 20% of patients developed oligospermia and 10% developed azoospermia. Seminal fluid parameters reverted back to normal after stoppage of hydroxyurea for 3 months in 73% of patients. CONCLUSIONS: Alteration of sperm parameters is seen in a significant number of sickle cell disease patients. Also, alterations of seminal fluid parameters are exacerbated by hydroxyurea treatment even with low dose. Therefore, treatment with hydroxyurea in adolescent and adult male sickle cell disease patients should be preceded by routine assessment of seminal fluid parameters and followed up regularly every 3 months for any change in seminal fluid parameters for evidence of hydroxyurea toxicity.

4. **Low dose hydroxyurea is effective in reducing the incidence of painful crisis and frequency of blood transfusion in sickle cell anemia patients from eastern India**

   2012

   Hemoglobin

   Patel, D K and Mashon, R S and Patel, S and Das, B S and Purohit, P and Bishwal, S C

There are several questions pertaining to dosage, duration and potential long-term toxicity of hydroxyurea (HU) therapy. Use of HU is extremely limited in eastern India because of its high cost and apprehension of its toxicities. We undertook this study to assess the clinical, biochemical and hematological efficacy of minimal dose HU (10 mg/kg/day) in 118 sickle cell anemia patients (27 pediatric and 91 adults). The frequency of painful crises reduced significantly in 71.5 and 92.2 in pediatric and adult cases, respectively. Ninety-five percent of the patients became transfusion independent. The baseline Hb F, total hemoglobin (Hb), MCV, MCH and MCHC levels increased significantly, whereas the WBC, platelet count and total serum bilirubin values decreased significantly. This is

the first study of minimal dose HU therapy in eastern India that showed impressive improvement in clinical and hematological parameters with minimal toxicity. Â© 2012 Informa Healthcare USA, Inc.

5. **Intravenous Acetaminophen vs Intravenous Diclofenac in the Management of Painful Crisis in Sickle Cell Disease: Authors' Reply**

   2021

   Indian pediatrics

   Mishra, N R and Kumar, R and Tripathy, S K and Mishra, N R

REVIEWS

1. **A Review of Automated Methods for the Detection of Sickle Cell Disease**

   2020

   IEEE Reviews in Biomedical Engineering

   Das, P K and Meher, S and Panda, R and Abraham, A

Detection of sickle cell disease is a crucial job in medical image analysis. It emphasizes elaborate analysis of proper disease diagnosis after accurate detection followed by a classification of irregularities, which plays a vital role in the sickle cell disease diagnosis, treatment planning, and treatment outcome evaluation. Proper segmentation of complex cell clusters makes sickle cell detection more accurate and robust. Cell morphology has a key role in the detection of the sickle cell because the shapes of the normal blood cell and sickle cell differ significantly. This review emphasizes state-of-the-art methods and recent advances in detection, segmentation, and classification of sickle cell disease. We discuss key challenges encountered during the segmentation of overlapping blood cells. Moreover, standard validation measures that have been employed to yield performance analysis of various methods are also discussed. The methodologies and experiments in this review will be useful to further research and work in this area.

CASE REPORTS

1. **Influence of rs1042713 and rs1042714 polymorphisms of Î²2-adrenergic receptor gene with erythrocyte cAMP in sickle cell disease patients from Odisha State, India.**

   2020

   Annals of Hematology

   Shalini, Sinha and Prasad, Jit Bimal and Kumar, Patro A Raj and Aisurya, Ray and Snehadhini, Dehury and Sarmila, Sahoo and Behera, Rajendra Kumar and Mohanty, Pradeep Kumar and Pinaki, Panigrahi and Padmalaya, Das and Sinha, Shalini and Jit, Bimal Prasad and Patro, A Raj Kumar and Ray, Aisurya and Dehury, Snehadhini and Sahoo, Sarmila and Behera, Rajendra Kumar and Mohanty, Pradeep Kumar and Panigrahi, Pinaki and Das, Padmalaya and Shalini, Sinha and Prasad, Jit Bimal and Kumar, Patro A Raj and Aisurya, Ray and Snehadhini, Dehury and Sarmila, Sahoo and Behera, Rajendra Kumar and Mohanty, Pradeep Kumar and Pinaki, Panigrahi and Padmalaya, Das and Sinha, Shalini and Jit, Bimal Prasad and Patro, A Raj Kumar and Ray, Aisurya and Dehury, Snehadhini and Sahoo, Sarmila and Behera, Rajendra Kumar and Mohanty, Pradeep Kumar and Panigrahi, Pinaki and Das, Padmalaya

   The vaso-occlusive crisis (VOCs) in sickle cell disease (SCD) is often associated with stress. Epinephrine released during stress acts via beta 2-adrenergic receptors (Î²2-AR or ADRB2) to stimulate the synthesis of cyclic adenosine monophosphate (cAMP) in the red blood cells (RBCs). Higher cAMP levels promote adhesion of sickled RBCs to vascular endothelium, a major contributor for VOCs. Several single-nucleotide polymorphisms (SNPs) of the Î²2-AR gene have been reported; two of them at codon 16 (rs1042713) and codon 27 (rs1042714) have been extensively studied for their clinical relevance. Therefore, we assessed the influence of polymorphism at these two sites of the Î²2-AR gene on the RBC cAMP concentrations with and without epinephrine stimulation in SCD subjects. We determined the frequency distribution of different genotypes of codon 16 and codon 27 of the Î²2-AR gene using the Sanger sequencing method in the SCD subjects. We measured the RBC-cAMP levels at baseline and after stimulation with epinephrine, to ascertain the influence of different genotypes in determining cAMP levels. There was no difference in the socio-demographic and hematological indicators in different genotypes of both codon 16 and 27. In the sham-treated erythrocytes, the cAMP levels were significantly different with three genotypes of codon 16 ($F = 3.39$, $P = 0.036$; one way ANOVA) but not with different genotypes of codon 27. A significant increase in cAMP levels was noticed with epinephrine treatment in all genotypes of codons 16 and 27 ($P = 0.001$; Wilcoxon signed-rank test). However, the extent of increase in the epinephrine-treated cAMP values from the sham-treated (baseline) cAMP values was significantly different between the three genotypes of codon 16 ($H = 8.74$; $P = 0.012$; Kruskal-Wallis test) but not in codon 27 genotypes. Polymorphism in codon 16 (rs1042713) of the Î²2-AR gene influences cAMP concentrations in the RBC both before and after epinephrine treatment. Higher cAMP levels may lead to increased adhesion of sickle cell RBCs to vascular endothelium and may increase the frequency of VOCs.

2. **Fetal Hemoglobin Modifies the Disease Manifestation of Severe Plasmodium Falciparum Malaria in Adult Patients with Sickle Cell Anemia**

   2016

   Mediterranean Journal of Hematology and Infectious Diseases

   Prasanta, Purohit and Siris, Patel and Mohanty, Pradeep Kumar and Padmalaya, Das and Jogeswar, Panigrahi and Purohit, P and Patel, S and Mohanty, Pradeep Kumar and Das, P and Panigrahi, J

Various African studies have shown that, even though SCA protects from P. falciparum infection, the risk of severe illness and death due to malaria is higher.2,3 Though several factors are responsible for the disease severity in P.falciparum malaria in patients with SCA, it was recently found that fetal hemoglobin (HbF), a physiological hemoglobin usually found higher in patients with SCA had a negative epistatic interaction with HbS during protection against malaria.4 The role of HbF against P. falciparum malaria in cases with normal hemoglobin genotypes has been widely studied and found to be protective against severe disease manifestation. [...]this protection afforded by alpha thalassemia becomes relatively sluggish when co-inherited with HbS. Because of a higher prevalence of alpha thalassemia in the study area,1 we have attempted to compare the hematological and clinical parameters in patients with heterozygous and homozygous alpha thalassemia separately against patients with normal alpha globin genotype. A large cohort study in a malaria endemic region is essential to give conclusive results on the association of HbF and use of hydroxyurea in patients with SCA. 1 Sickle Cell Clinic and Molecular Biology Laboratory, Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR), Burla, Sambalpur, Odisha, India 2 Department of Infectious Disease, Asian Institute of Public Health, Bhubaneswar, India 3 School of Life Sciences, Sambalpur University, Jyotivihar, Burla, Odisha, India

3. **Haptoglobin Genotypes Associated with Vaso-Occlusive Crisis in Sickle Cell Anemia Patients of Eastern India**

   2020

   Hemoglobin

   Meher, Satyabrata and Mohanty, Pradeep K and Patel, Siris and Das, Kishalaya and Sahoo, Sarmila and Dehury, Snehadhini and Mohapatra, Manoj K and Jit, Bimal P and Das, Padmalaya and Dash, Bisnu P

Sickle cell anemia is hallmarked by hemolysis, which releases hemoglobin (Hb) into the plasma promoting vaso-occlusive crisis (VOC). Haptoglobin (Hp) clears free Hb and decreases Hb-related pathophysiology in sickle cell anemia. There are two alleles (HP1 and HP2) and three genotypes (HP1-1, HP1-2 and HP2-2) of Hp with different frequencies in different populations. This study involved Hp level and genotype among normal and sickle cell anemia patients with varying severity of VOC. A total of 297 sickle cell anemia patients and 98 healthy controls were selected for the study. The sickle cell anemia patients were categorized as â€˜mild-phenotypeâ€™ with no pain episodes and â€˜severe-phenotypeâ€™ as having three or more acute pain episodes in the preceding 12 months. The Hp level was significantly lower ($p < 0.001$) in sickle cell patients anemia than controls; HP1-1 genotype had a higher Hp level compared to HP1-2 and HP2-2 ($p < 0.05$). Turkey-Kramer multiple comparison tests showed that mild and severe phenotypes have significant differences ($p < 0.05$) in Hb F%, Hb, platelet count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), direct-bilirubin (Bil-D), total-bilirubin (Bil-T), lactate dehydrogenase (LDH) and Hp level. Pearson correlation revealed that Hp level has a positive ($p < 0.05$) correlation with Hb F%, Hb, packed cell volume (PCV) and serum urea; in contrast its level is negatively correlated with AST, ALT, Bil-T and LDH. A significantly higher frequency of HP2 allele and HP2-2 genotypes was found in severe phenotypes. In the studied population, it was found that higher HP2 frequency, low Hp level and more hemolysis favors the onset of VOC in sickle cell anemia.

4. **Genetic marker profile of primitive Kutia Kondh tribal population of Phulbani district (Orissa)**

   1995

   Indian Journal of Medical Research

   Basu, S and Jindal, A and Kumar, C S and Khan, A S

Blood samples from 330 Kutia Kondhs (a primitive tribal population of Orissa) were subjected to a battery of tests for genetic markers to find out the incidence of various blood group polymorphisms (ABO, MN, Duffy, JKa), serum proteins, sickling and G-6-PD deficiency. Predominance of O (39.09%) blood group for ABO, N blood group (53.44) for MN and Fya+b+ (55.72) for Duffy blood group, were observed. High incidence of Hp2.1

(39.33), SS (70.43) and CC (96.65) for haptoglobulin, C, and transferrin respectively were seen. The overall frequency of sickling was observed to be 16.36 per cent. The sex-wise distribution of G-6-PD was 13.71 per cent for males and 1.84 for females.

5. **Molecular hematological and clinical characterization of sickle cell HBE in eastern India: The largest series in world**

   2014

   Indian Journal of Hematology and Blood Transfusion

   Patel, S and Meher, S and Dehury, S and Purohit, P and Das, K and Patel, D K and Mohanty, P K

Summary: This is the first report of a large cohort (14 cases) of HbSE double heterozygote state from Odisha, India. Patients with HbSE presents varied clinical manifestations. Introduction: Sickle Cell Disease (SCD) is the commonest hemoglobin disorder in Eastern India. Co-inheritance of Hb E (cd26, Glu> Lys, GAG> AAG), with HbS (HbSE) presented with varied clinical presentation ranging from asymptomatic to severe disease. Materials and Methods: Sickling test, alkaline electrophoresis, CBC, Biochemical examination, CEHPLC were carried out at Sickle Cell Clinic & Molecular Biology Laboratory, VSS Medical College&Hospital, Burla, Odisha. HbS/HbE mutation characterized by ARMS-PCR/RFLP & DNA sequencing. Xmnl polymorphism and Î±-thalassemia were done by PCR. HbSE cases compared with matched HbSÎ²-thalassemia and HbSS. Results: Fourteen HbSE cases revealed HbE (31.69 Â± 4 %) eluting at HbA2 window (RT 3.75 Â± 0.01) and HbS 57.35 Â± 3.15 (RT 4.44 Â± 0.01) in CE-HPLC. DNA sequencing confirmed HbS mutation at codon-6 (GAG> GTG) and HbE at codon-26 (GAG> AAG). Rate of VOC and Blood-Transfusion were lower in HbSE, where as incidence of splenomegaly, AVN and cholelithiasis were comparable. MCV, MCH and MCHC were lower than HbSS and higher than HbSb. All biochemical parameters were lower in HbSE compared to both HbSÎ² and HbSS patients. Six cases are on Hydroxyurea therapy (10 mg/kg/day). Six cases were co-inherited with Î±-thalassemia (three Î±-3.7 and three Î±-4.2) in heterozygous state. Xmnl polymorphism was found in HbSE cases. Conclusion: This is the first report on 14 cases of HbSE, the largest number of subjects studied. HbSE patients presented with microcytic-hypochromic blood picture and clinically less severe compared to both HbSÎ² and HbSS patients.

6. **The molecular basis of Î± thalassemia in India. Its interaction with the sickle cell gene**

   1988

   Blood

   Kulozik, A E and Kar, B C and Serjeant, G R and Serjeant, B E and Weatherall, D J

The Î± globin genotype of a total of 282 Indians from Orissa state has been analyzed. The overall Î± thalassemia gene frequency is 0.29, most frequently caused by the -Î±3.7 and -Î±4.2 deletions. In one family a novel -Î±3.5 deletion removing the Î±1 globin gene with some of its flanking sequences has been found, suggesting further sequence homology of the Î± globin gene cluster 3' to the Î±1 globin gene. Patients with sickle cell disease and Î± thalassemia had higher hemoglobin (Hb) levels, RBC counts, and Hb A2 levels, and lower reticulocyte counts, MCV, MCH, and Hb F levels than those with a normal Î± genotype. The frequency of splenomegaly was not influenced by the Î± globin genotype. A higher prevalence of Î± thalassemia was found in patients â‰¥ 10 years of age than in the younger group, suggesting a possible advantageous effect of Î± thalassemia on the survival of patients with sickle cell disease.

7. **Comparative study of clinical presentation and hematological indices in hospitalized sickle cell patients with severe Plasmodium falciparum malaria**

   2018

   Journal of Infection and Public Health

   Purohit, P and Mohanty, P K and Patel, S and Das, P and Panigrahi, J and Das, K

Background: Sickle-cell-gene has a high frequency in malaria endemic regions. In India, though the prevalence of both sickle-cell-gene and malaria are high, no study has been carried out. This study aims to find out the possible differences in hematological and clinical parameters in severe falciparum malaria with respect to sickle cell genotypes. Methods: Five hundred fourteen adults with severe falciparum malaria hospitalized in Department of Medicine, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, between August, 2010 to December, 2014 were included and categorized on the basis of sickle cell genotypes. The hematological parameters were compared by one-way-analysis-of-variance and incidence of sub-phenotypes of severe malaria was compared by Ï‡2 test across the groups. Results: Patients with sickle cell anemia (HbSS) and severe falciparum malaria had lower hemoglobin level compared to patients with normal Î²-globin genotype (HbAA) and sickle cell trait (HbAS). Most of the hematological parameters were homogeneous in patients with HbAA and HbAS and different from patients with HbSS. Incidence of acute renal failure was low (Ï‡2, 9.91; p, 0.002) and jaundice was high (Ï‡2, 5.20; p, 0.022) in patients with HbSS. No clinical difference was observed in patients with HbAA and HbAS. The mortality was low (Ï‡2, 4.33; p, 0.037) and high (Ï‡2, 10.48; p, 0.001) in patients with HbAS and HbSS respectively compared to patients with HbAA. Conclusion: Though sickle-cell-gene protects against falciparum infections, the hematological parameters and sub-phenotypes of severe malaria remain unchanged when the infection progresses to a severe form in patients with HbAA and HbAS. Presence of hemolytic anemia in patients with HbSS shows diverse hematological and clinical phenotypes as compared to others. High mortality in patients with HbSS emphasizes the need for a better preventive approach to save valuable lives.

8. **Fetal hemoglobin levels and beta (s) globin haplotypes in an Indian populations with sickle cell disease.**

   1987

   Blood

   Kulozik, A E and Kar, B C and Satapathy, R K and Serjeant, B E and Serjeant, G R and Weatherall, D J

To further explore the cause for variation in hemoglobin F (Hb F) levels in sickle cell disease, the beta globin restriction-fragment length polymorphism haplotypes were determined in a total of 303 (126 SS, 141 AS, 17 S beta(0), 7 A beta, (0) and 12 AA) Indians from the state of Orissa. The beta(s) globin gene was found to be linked almost exclusively to a beta(S) haplotype (-++-), which is also common in Saudi Arabian patients from the Eastern Province (referred to as the Asian beta(s) haplotype). By contrast, the majority of beta A and beta(0) thalassemia globin genes are linked to haplotypes common in all European and Asian populations (+-----[+/-]; --++-++). Family studies showed that there is a genetic factor elevating Hb F levels dominantly in homozygotes (SS). This factor appears to be related to the Asian beta(s) globin haplotype, and a mechanism for its action is discussed. There is also a high prevalence of an independent Swiss type hereditary persistence of fetal hemoglobin (HPFH) determinant active in both the sickle cell trait and in sickle cell disease.

9. **Î²-globin gene haplotypes linked with the Hb D-Punjab [Î²121(GH4)Gluâ†'Gln, GAA>CAA] mutation in eastern India.**

   2010

   Hemoglobin

   Patel, Dilip K and Mashon, Ranjeet S and Patel, Siris and Dash, Preetinanda M and Das, Bhabani S

Hb D-Punjab [Î²121(GH4)Gluâ†'Gln] is prevalent in the northern states of the Indian subcontinent. Due to inadequate data from Asian countries, the origin and spread of the Hb D-Punjab mutation are uncertain. In a study of sickle cell hemoglobinopathies, we detected the Hb D-Punjab mutation in 25 subjects from 11 unrelated Agharia families. Twelve cases were Hb S [Î²6(A3)Gluâ†'Val]/Hb D-Punjab compound heterozygotes and 13

were Hb D trait carriers. In 76.0% of the cases, the Î²(D) gene was linked to haplotype I, whereas 24.0% had a novel haplotype. None of the haplotypes matched the Î²(A) haplotype of the local population. In view of the ancestral origin of the subjects and the high prevalence of the Î²(D) gene in the states of northern India, we suggest a North Indian origin for the Î²(D) mutation in our population. The finding of a novel haplotype in eastern India supports the hypothesis of a multicentric origin of this mutation.

10. **Geographical survey of Î²(S)-globin gene haplotypes: Evidence for an independent Asian origin of the sickle-cell mutation**

    1986

    American Journal of Human Genetics

    Kulozik, A E and Wainscoat, J S and Serjeant, G R

The haplotypes of 152 Î²(S)-chromosomes were characterized in six different population groups. The chromosomes of individuals from Nigeria and from the southwest of the Arabian peninsula have the haplotype ----+ +-+ previously found in west African, Jamaican, and U.S. American blacks, whereas those from the eastern oases of Saudi Arabia and from the west and the east coast of India showed a different haplotype not found in Africa (++-++ ++-). These data are most consistent with an independent Asian origin of the sickle-cell mutation and provide further information about the geographic distribution of Î²(S)-haplotypes in the Old World. The distribution of the Asian Î²(S)-haplotype corresponds to the reported geographic distribution of a mild clinical phenotype of homozygous SS disease.

11. **Erythrocyte cAMP in Determining Frequency of Acute Pain Episodes in Sickle Cell Disease Patients from Odisha State, India**

    2019

    Hemoglobin

    Jit, B P and Mohanty, P K and Pradhan, A and Purohit, P and Das, K and Patel, S and Meher, S and Sinha, S and Mohanty, J R and Behera, R K and Das, P

Vaso-occlusive crisis (VOC) occurs more frequently during stress in sickle cell disease patients. Epinephrine released during stress increases adhesion of sickled red blood cells (RBCs) to endothelium and to leukocytes, a process mediated through erythrocyte cyclic adenosine monophosphate (cAMP). Increased adhesion of sickled RBCs retards blood flow through the capillaries and promotes vaso-occlusion. Therefore, we examined the association of RBC-cAMP levels with frequency of acute pain episodes in sickle cell disease subjects. Using a case control study design, we measured RBC-cAMP levels, fetal hemoglobin (Hb F), Î±-thalassemia (Î±-thal) and other hematological parameters at baseline (sham treated) and after stimulation with epinephrine. The cases consisted of sickle cell disease subjects with three or more acute pain episodes in the last 12 months, and those without a single acute pain episode in the last 12 months were considered as controls. Significantly higher cAMP values were found in cases than the controls, in both sham treated ($p < 0.001$) and epinephrine treated RBCs ($p < 0.001$) by Wilcoxon Rank Sum test. However, significant association of cAMP values was observed both on univariate [odds ratio (OR): 4.8, 95% confidence interval (95% CI): 1.51-15.19, $p < 0.008$) and multivariate logistic regression analyses only in epinephrine treated (OR: 5.07, 95% CI: 1.53-16.82, $p < 0.008$) but not in sham-treated RBCs. In the covariates, Hb F consistently showed protective effects in univariate as well as in multivariate analyses. Frequent acute pain episodes are associated with higher cAMP levels than those with less frequent pain episodes, only after stimulation with epinephrine but not with baseline level.

12. **Vitamin A status and hematological values in sickle cell disorder cases.**

    2012

    Indian Journal of Medical Sciences

    Behera, Shuchismita and Dixit, Sujata and Bulliyya, Gandham and Kar, Shantanu Kumar

Background: Sickle cell anemia (SCA), which is an inherited blood disorder characterized primarily by chronic anemia and oxidative stress plays a major role in pathophysiology.Objective: This study aims to evaluate vitamin A (serum retinol) status and hematological parameters in children with homozygous and heterozygous sickle cell disorders and compared with age- and sex-matched healthy controls.Materials and Methods: A sample of 80 referred cases (37 sickle cell disorders and 43 normal cases) aged 2-40 years were included in the study. Hematological parameters were measured in cell counter and serum retinol by high-performance liquid chromatography.Results: The mean hemoglobin (Hb) and serum retinol were significantly lower among cases with sickle cell disease than in sickle cell trait and normal. Vitamin A deficiency (retinol < 20 Î¼g/dl) reported to be higher in homozygous cases (46.2%) as compared to either heterozygous (29.2%) or control (23.2%) groups. Serum retinol was correlated directly with Hb, RBC count, and hematocrit levels, and inversely with percentage of sickling among sickle cell disorder cases.Conclusion: The results indicate that deprived vitamin A status with inductive oxidative stress is mainly due to sickling and hemolysis in SCA cases.

13. **Association of plasma homocysteine level with vaso-occlusive crisis in sickle cell anemia patients of Odisha, India.**

    2019

    Annals of Hematology

    Meher, Satyabrata and Patel, Siris and Das, Kishalaya and Dehury, Snehadhini and Jit, Bimal Prasad and Maske, Mahendra M and Das, Padmalaya and Dash, Bisnu Prasad and Mohanty, Pradeep Kumar

Vascular complications of sickle cell anemia (SCA) are influenced by many factors. Elevated plasma homocysteine (Hcy) is supposed to be an independent risk factor and is either genetic or nutritional origin. The present study evaluated the plasma Hcy level, MTHFR C677T gene polymorphism, effect of folic acid (FA) supplementation' and hemato-biochemical parameters in SCA and their effect on the vaso-occlusive crisis (VOC) in SCA patients of an Asian-Indian haplotype population. One hundred twenty cases of SCA (HbSS) and 50 controls with normal hemoglobin(HbAA) were studied. It was found that the plasma Hcy level is significantly higher (pâ€‰<â€‰0.0001) in patients with SCA (22.41â€‰Â±â€‰7.8Â Î¼mol/L) compared to controls (13.2â€‰Â±â€‰4.4Â Î¼mol/L). Moreover, patients without FA supplementation had a significantly (pÂ <â€‰0.001) higher Hcy level (27â€‰Â±â€‰7Â Î¼mol/L) compared to those with supplementation (17.75â€‰Â±â€‰5.7Â Î¼mol/L). Turkey-Kramer multiple comparison tests show that there is a significant difference (pâ€‰<â€‰0.05) in HbF percent, hemoglobin (Hb), platelet count, serum bilirubin (direct:Bil-D and total:Bil-T), aspartate transaminaseÂ (AST), lactate dehydrogenase (LDH), and plasma Hcy levels between mild and severe VOC. Between moderate VOC and severe VOC, there was a significant difference (pâ€‰<â€‰0.05) in HbF%, Bil-D, AST, Hcy. Pearson correlation revealed that plasma Hcy had a significantly (pâ€‰<â€‰0.05) positive correlation with AST, serum bilirubin (indirect and total), LDH, jaundice, stroke, VOC per year, and hospitalization per year whereas it was inversely correlated with HbF percentage, Hb level, and FA treatment. In the study population, increased plasma Hcy level, hemolysis, and platelet activation were found to influence VOC in SCA.

14. **Comparative analysis of haematological and endothelial dysfunction in HBSB 11t and sickle cell disease (SCD) variants of tertiary care hospital of odisha**

    2020

    Indian Journal of Hematology and Blood Transfusion

    Dutta, S and Kar, B and Mohanty, P K and Nayak, R K

Aims & Objectives: In sickle cell disease and HbSÎ² .++T, hematological variation pose a great threat to the well-being of endothelial cells, thus causing endothelial dysfunction. This may lead to various clinical complications including vaso-occlusive crisis (VOC), splenic sequestration, osteomyelitis, acute chest syndrome (ACS);etc. This study was done to analyse the correlation between the hematological parameters and endothelial dysfunction in children with an age range of 10.07 Â± 0.17 in boys and 11.7 Â± 0.24 in girls. Patients/Materials & Methods: The patients attending the out-patient department (OPD) of Hematology and Paediatrics, Sri Ram Chandra Bhanja Medical College and Hospital (SCBMCH), Cuttack, India were screened. To select the number of standard population or sample size, the statistical formula proposed by Yamane was used. Cohort method of analysis was used where clinical reports and questionnaire were used to analyse the symptomatic parameter in the patients. : Children with Hb-S-Î²-thalassemia who were within the inclusion criteria and attending the OPD were first educated about the procedure and then the same procedure was also explained to their parents. The consent of the parents was taken on the consent form as maximum patients selected were minor in age. For comparative analysis, one way ANOVA with p>0.05 level of significance was considered. Results: When hematological parameters were analysed it was observed that there was no significant variation in HbA % in HbSÎ² .++T variants whereas in SCD patients a decline was observed in both the sexes. HbA2% and HbF % was slightly increased inn both the variants whereas in SCD patients, there was an increase in HbS % with significant variation. HCT % showed gradual decrease in both the variants with modif decrease in the Hb (gmdl-1). A significant decrease was also observed in MCH (pg) and MCV (fL) with signifies the presence of abnormal erythropoietic cells. A significant decrease in the flow mediated vasodilation (FMD) was observed in SCD whereas a moderate decrease was observed in HbSb . ++T variants, thus, indicating endothelial dysfunction. Discussion & Conclusion: In the present study, correlation was observed in the decrease in the FMD values and clinical manifestations among the patients which indicates impairment in erythropoiesis.

15. **Sickle cell 'D' disease - A case report from Orissa.**

    2000

    Indian Journal of Hematology and Blood Transfusion

    Pati, S and Sahu, S and Rath, P K

Sickle cell 'D' disease is a double heterozygous state of sickle cell as well as HbD Punjab, which is a rare presentation. We report a case of six-year-old boy presenting with hemolytic anemia having sickle cell Punjab.

16. **A rare dominant beta thalassaemia mutation in association with HBS: First report of Hbwestdale (CD.126-131:17 BP deletion) from Odisha, India**

    2014

    Indian Journal of Hematology and Blood Transfusion

    Dehury, S and Sarkar, B and Pate, D K and Meher, S and Purohit, P and Jana, A and Bhattacharya, S and Das, K and Mohanty, P K and Patel, S

Summary: FS-17bp-del (HbWestdale) in Î²-Globin-gene produces severe Î²0-thalassaemia. We carried out clinico-haematological comparison of four cases of HbS/HbWestdale double heterozygote with matched HbS-Î²-Thalassaemia with IVS-I-5-G> C mutation and HbSS patients from Odisha. The findings agree to earlier

inferences on HbWestdale from Trinidad and Pakistan. Introduction: We report here the first series of severe SCD with 17 bp deletion b0-thalassaemia (Hb-Westdale, Cd. 126-131, -17bp-del), hitherto unreported from Odisha. Detailed study of clinico-haematological characterisation of 4 HbS/HbWestdale agreed to earlier reports of Î²-thalassaemia with this mutation. The finding has implications in PND of SCD in India. Materials and Methods: Screening with haematological, biochemical-investigations and parent-screening revealed large cohort of HbS-Î²-thalassaemia during 2011-2014 under Odisha Sickle Cell Project (NHM). Mutation confirmation of HbS and Î²-thalassaemia were done by ARMS-PCR and DNA Sequencing. Clinico-haematological data of matched HbSS and HbS/Î²-Thalassaemia (IVS-I-5- G> C mutation) patients has been done. Results: Four of seven HbWestdale cases had co-inherited HbS. HbA0, MCV, MCH and TPC were significantly lower in HbS/HbWestdale cases compared to both HbS/Î²-thalassaemia [IVS1-5(G â†' C) mutation] and HbSS. HbS/HbWestdale patients had more painful episodes than that in both HbS/Î²-thalassaemia [IVS1-5(G â†' C) mutation] and HbSS patients, where as blood transfusion among them was similar with HbSS patients. Hepato-splenomegaly was common clinical presentation. Higher LDH in HbS/HbWestdale imply the possible increased haemolysis consequent to the instability of the HbWestdale tetramer and corroborates to the earlier reports. Conclusion/Diagnosis/ Impression: This is the first report describing four patients with HbS/ HbWestdale in literature. We found that SCD with HbWestdale present severe clinical manifestation compared to patients with other HbS/Î²-thalassaemia types.

17. **A study of the glucose uptake, pyruvate and lactate formation in red blood cells of normal, sickle cell trait and sickle cell patients**

    1992

    Indian Journal of Clinical Biochemistry

    Dash, B P and Mittra, A and Kar, B C

18. **Spectrum of hemoglobinopathies in the state of orissa: A ten years cohort study**

    2006

    Journal of Association of Physicians of India

    Singh, A K

19. **A pair of dizygotic twins born to two carrier families of sickle cell disease in scheduled caste communities of Orissa, India.**

    2009

    Special Issue: Rural Health

    Balgir, Ranbir S and RS, Balgir

The sickle cell disease is a genetically inherited commonly encountered hematological disorder in the state of Orissa. It causes high degree of morbidity, mortality and fetal wastage in the poor vulnerable people. For the first time, a carrier couple of sickle cell disease had delivered twin offspring with carrier as well as the homozygous sickle cell disease or homozygous sickle cell disease and normal offspring. The suspected cases of hemoglobinopathies suffering from anemia are routinely referred from different peripheral Primary Health

Centres (PHCs) and hospitals in the state of Orissa to our centre for detailed investigations and genetic/marriage counseling. Out of these referral cases, two scheduled castes, i.e. Domb and Pana, families with twin children were referred from Kalahandi and Kandhamal districts of Orissa, respectively and were studied in details. The present study reports for the first time a rare occurrence of dizygotic twins (sickle cell trait and sickle cell disease in one family and sickle cell disease and normal child in another family) in a singleton pregnancy in the sickle cell carrier parents, respectively from Kalahandi and Kandhamal districts of Orissa, India. It is true that twin gestation does not change the preconception probability, but this study clearly shows co-existence of two different genotypes in a singleton pregnancy. It is a rare occasion when a single pregnancy carries either two or more distinct abnormal genotypes at a time in a womb in human beings. Dizygotic twins are genetically different and, thus, provide means of appraisal of the expression of different genotypes under the same environmental conditions.

20. **Type 1 diabetes mellitus in homozygous sickle cell anaemia**

    2005

    Journal of Association of Physicians of India

    Mohapatra, M K

For reasons unknown, the association of diabetes mellitus with sickle cell anaemia is uncommon. A patient of sickle cell anaemia with diabetes mellitus, complicated with ketoacidosis is being reported in view of its rarity. Â© JAPI 2005.

21. **Cutaneous manifestation of sickle cell disease**

    2021

    Journal of Applied Hematology

    Patnayak, R and Das, P and Patra, S and Bhola, R K

Sickle cell disease (SCD) is an autosomal recessive hemoglobinopathy. SCD patients commonly present with skin ulceration. This case is about a 22-year-old male whose initial presentation was reddish spots on both lower legs. Skin biopsy revealed features of leukocytoclastic vasculitis with sickled red blood cells (RBCs). He was further evaluated with sickling test which was positive. His hemoglobin electrophoresis was reported as sickle-beta thalassemia. This case is presented to emphasize the importance of RBC morphology and high index of suspicion, particularly in dealing with patients from the sickle cell belt area.

22. **Renal derangement in sickle cell anemia during vaso-occlusive crisis: Report of 4 cases**

    2019

    Indian Journal of Hematology and Blood Transfusion

    Pandey, J and Mohanty, D and Das, S and Jagati, S

Aims & Objectives: AIMS: Paucity of reports regarding renal derangement in sickle cell anemia cases prompted us to undertake this present study. This will help us in taking necessary timely interventions in affected cases of

SCD. Objective: To find out whether the kidney functions are altered in homozygous sickle cell disease cases during vaso-occlusive crisis. Patients/Materials & Methods: The present case report includes 4 sickle cell anemia cases, who have moderate to severe renal involvement during vaso-occlusive crisis, presented at Apollo hospitals from June 2018 to July 2019. They were treated accordingly. After the proper management all the cases recovered and they are on follow up. Results: All 4 were sickle cell anemia (ss) cases who presented with renal derangement, during their vaso-occlusive crisis (Table 1). Discussion & Conclusion: This present study brings out the fact that renal involvement during sickle cell crisis is not uncommon. However one has to look for the renal derangement so that proper timely management of the same can be undertaken for recovery of the cases. This study also stresses the utility of routine and microscopic urine examination of SCD patients for early detection of renal involvement, during follow up of the cases in O.P.D. (Table Presented).

23. **Hb Tianshui (HBB: C.119A > G) in Compound Heterozygosity with Hb S (HBB: C.20A > T) from Odisha, India**

    2016

    Hemoglobin

    Meher, S and Dehury, S and Mohanty, P K and Patel, S and Pattanayak, C and Bhattacharya, S and Das, K and Sarkar, B

We describe here a rare Î²-globin gene variant, Hb Tianshui [Î²39(C5)Gluâ†'Arg; HBB: c.119A > G], detected during routine screening in Odisha, India. This is the second report of Hb Tianshui and the first to describe the cation exchange high performance liquid chromatography (HPLC) and DNA studies of two cases of this variant. Both cases had coinherited Hb S (HBB: c.20A > T) but none presented with typical symptoms of sickle cell disease. One of the cases was heterozygous for a common Î±-thalassemia (Î±-thal) allele (âˆ'Î±3.7) (rightward) (NG_000006.1: g.34164_37967del3804) and marginally raised Hb F percentage, while the other Hb S/Hb Tianshui case was completely benign and healthy. An atypical Asian Indian haplotype [+ âˆ' + âˆ' +] could be assigned to the Hb Tianshui variant. Hb Tianshui seems to mimic a few other Hb variants in cation exchange HPLC. However, we report two specific patterns in the chromatograms that are characteristic to Hb Tianshui. Combining an alkaline electrophoresis result with cation exchange HPLC at screening would be preferred to detect this rare variant, especially in regions with considerable frequency of Hb E [Î²26(B8)Gluâ†'Lys; HBB: c.79G > A] or Hb S.

24. **Compound Heterozygote of Hb S (HBB: c.20A>T)/Hb Westdale (HBB: c.380_396delTGCAGGCTGCCTATCAG): Report of Four Cases from Odisha State, India.**

    2019

    Hemoglobin

    Dehury, Snehadhini and Meher, Satyabrata and Patel, Siris and Das, Kishalaya and Jana, Arpita and Bhattacharya, Subhra and Sahoo, Sarmila and Sarkar, Biswanath and Mohanty, Pradeep K

We report four cases of compound heterozygotes for Hb S (HBB: c.20A>T) and a rare Î²(0)-thalassemia (Î²(0)-thal) mutation, Hb Westdale (HBB: c.380_396delTGCAGGCTGCCTATCAG), characterized by a 17â€‰bp deletion between codons 126 to 131 in exon 3 of the Î²-globin gene of human hemoglobin (Hb) confirmed by direct Î²-globin gene sequencing. All four cases were from four unrelated families belonging to the Agharia caste, an endogamous ethnic community of the Sundargarh and Jharsuguda districts of Odisha State, India. Detailed observations indicated that all four cases of Hb S/Hb Westdale were clinically severe. On family screening, six family members were found to be heterozygous for Hb Westdale and were asymptomatic. Deletional Î±-thalassemia (Î±-thal) and XmnI polymorphism were studied for all the Hb Westdale cases. The Hb S/Hb Westdale cases had an early median age at onset of symptoms and presentation, more requirement of blood transfusions, splenomegaly and hepatomegaly and were found to be clinically more severe when compared with the Hb S-Î²-thal with IVS-I-5 (G>C) (HBB: c.92â€‰+â€‰5G>C) cases. Overall, the findings indicate that this rare and hitherto unreported compound heterozygosity of Hb S/Hb Westdale is a clinically significant hemoglobinopathy and its finding in a large endogamous community of Odisha State, India will have important implication in the epidemiology and understanding of the clinical spectrum of sickle cell disease in Indian context and prenatal diagnosis.

OTHERS

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1. **Hematoma; Reports from Department of Neurosurgery Describe Recent Advances in Hematoma (Spontaneous extradural and subgaleal hematoma: A rare neurosurgical crisis of sickle cell disease)**

   2017

   Health & Medicine Week

According to news reporting originating from Cuttack, India, by NewsRx correspondents, research stated, "Extradural hematoma (EDH) in absence of trauma is a rare entity with only few cases reported in literature. Vascular malformation of dura, coagulopathies, sinus infection, middle ear or orbital infection, and tumor." According to the news editors,...

2. **Beneficial Effect of Low Fixed Dose of Hydroxyurea in Vaso-occlusive Crisis and Transfusion Requirements in Adult HbSS Patients: A Prospective Study in a Tertiary Care Center**

   2018

   Indian Journal of Hematology and Blood Transfusion

   Sethy, S and Panda, T and Jena, R K

Significant reduction in morbidity and mortality have been documented in patients with sickle cell disease (HbSS) by most of the studies using hydroxyurea at a dose of 25â€“35Â mg/kg/day or maximum tolerated dose. But toxicities, need for frequent monitoring, compliance and cost are important hurdles particularly in Indian set up. We undertook this study to find out the efficacy, safety compliance rate of low fixed dose of hydroxyurea (10Â mg/kg/day) in patients presenting to our hospital and its impact on clinical profile and laboratory parameters. A cohort of 128 (82 males, 46 females) confirmed HbSS cases (each >18Â years age, vaso-occlusive crisis >2/years and/ or rate of transfusion 1â€“2Â units/month) with no disease related end organ damage were assessed prospectively between 2013 and 2016. They were started on 10Â mg/kg/day hydroxyurea along with other supportive care and followed up monthly for 1Â year. Clinical and laboratory parameters before and after therapy were reviewed and compared. In 92% of cases presenting with repeated vaso-occlusive crisis, VOC disappeared completely during follow up and in 8% we found significant reduction in severity as well as frequency of attacks (pÂ <Â 0.01). Again in 87%, no further transfusion was required during follow up and in 13%, it further reduced the rate of transfusion (pÂ <Â 0.01). The median time of response for VOC was 3Â months and in transfusion requirement was 5Â months. There was also significant reduction in S.Billirubin, S.LDH, disease related complications and rate of hospitalisation with significant improvement in Hb, MCV, and MCH. There is insignificant increase in HbF with median (1.5â€“2.4)% and in 5 cases >5%. We did not find any remarkable adverse effect of the drug during the study period. Low fixed dose hydroxyurea (10Â mg/kg/day) is beneficial in reducing the vaso-occlusive crisis and transfusion requirement in adult HbSS Patients (Arab-Indian Haplotype). It is safe, suitable and is a effective mode of treatment in resource poor setting like India.

3. **A prospective study to compare the maternal and fetal outcomes among sickle cell disease and trait women**

   2019

   Journal of SAFOG

   Dora, S K and Dandapat, A B and Pande, B and Bhoi, G and Tiwari, B

Introduction: We conducted a prospective trial to compare the maternal and fetal outcomes between the sickle cell disease (SCD) and sickle cell trait (SCT) pregnant patients. Materials and methods: From December 2015 to

December 2016, a total of 59 patients were diagnosed with SCD and 119 patients with SCT. All the fetal and maternal parameters were compared between them. Results: A total of 17 (28.8%) SCD and 5 (4.2%) SCT patients presented with painful crisis. Acute chest syndrome developed in 9 (15.3%) of SCD and 1 (0.8%) of SCT cases. Hemolytic crisis was seen in 4 (6.8%) of SCD patients. The incidence of hypertension, preeclampsia, jaundice, blood transfusion during pregnancy, and IUGR among the SCD and SCT patients were 11 (18.6%) vs 5 (4.2%) (p = 0.000), 19 (32.2%) vs 7 (5.9%) (p = 0.000), 15 (25.4%) vs 0 (0%) (p = 0.000), 36 (61%) vs 8 (6.7%) (p = 0.000), and 33 (55.9%) vs 21 (17.6%) (p = 0.000), respectively. The mean periods of gestation of delivery were significantly lower, i.e., 36.5 Â± 2.76 weeks for SCD patients compared to 38.2 Â± 2.1 weeks for SCT patients (p = 0.000). Ten (16.9%) of SCD and one (0.8%) of SCT patients had intrauterine death. Average birth weights of babies delivered were 2142 Â± 557.45 g and 2684 Â± 551.23 g for SCD and SCT patients, respectively. Conclusion: Sickle cell anemia causes an increased risk to both mother and fetus. Sickle cell disease women are more prone to develop sickle cell crisis as well as increased obstetrical complication. A preconceptional counseling of all sickling women with a multidisciplinary approach can prevent many of the maternal and fetal complications during pregnancy.

4. **Coagulation profile in pathophysiology of sickle cell anemia**

   2020

   National Journal of Physiology, Pharmacy and Pharmacology

   Shehin, M and Purohit, K C and Jena, S K and Basila, V

Background: Sickle cell anemia (SCA) is an emerging public health challenge in India as well as globally. The WHO recognized it as a global problem since long time. In Western Odisha, its prevalence varies from 5% to 30%. Aim and Objective: The objective of this study was to determine the alteration of the coagulation profile in SCA in comparison to healthy control. Materials and Methods: This study was completed with 60 subjects that included 30 cases and 30 controls. This study was approved by the Institutional Ethical Committee. The hematological parameters such as bleeding time, clotting time, total platelet count, prothrombin time (PT), and activated partial thromboplastin time (aPTT) were tested. The data were analyzed through SPSS 20. Results: In this study, it was found that patients with SCA have increased clotting time (P = 0.007), PT (P = 0.000), aPTT (P = 0.003), and total platelet count (P = 0.183), but decreased bleeding time (P = 0.000) in comparison to healthy control. Conclusion: We found a significant increase in clotting time, PT, and aPTT, but decrease in bleeding time in SCA patients in comparison to healthy adults.

5. **Fetal hemoglobin and alpha thalassemia modulate the phenotypic expression of HbSD-Punjab**

   2014

   International Journal of Laboratory Hematology

   Patel, D K and Purohit, P and Dehury, S and Das, P and Dutta, A and Meher, S and Patel, S and Bag, S and Mashon, R S and Das, K

Introduction: HbSD-Punjab (HbSD) is a less common form of sickle cell disease (SCD) and discrimination between HbSD and HbSS is not possible on alkaline electrophoresis because the two variants overlap in the

compound heterozygous state. There are only a few publications consisting mostly of case reports. Thus, the phenotypic expression of HbSD and its modifiers has not been studied. Methods: We studied the phenotypic expression of 42 cases of HbSD (the largest number of subjects ever included in this kind of study) and compared them with 84 HbSS cases matched for age, sex, and caste. Further, we evaluated the influence of HbF concentration and alpha thalassemia on the phenotypic expressions of HbSD, namely the frequency of VOC and degree of hemolysis. Results: The frequencies of VOC were similar in both the groups. The markers of hemolysis such as total bilirubin, unconjugated bilirubin, and LDH were higher where as HbF concentration was significantly low in HbSD. There was a negative correlation between HbF concentration and risk of VOC in the HbSD. The total hemoglobin level and hematocrit were significantly high, and the MCV and MCH were significantly low in HbSD with alpha thalassemia. Alpha thalassemia had no influence on the frequency of VOC and severity of hemolysis in HbSD. Conclusion: HbF reduced the frequency of VOC but had no influence on the hemolytic markers in HbSD. HbSD with alpha thalassemia was associated with hypohromic and microcytic features of red blood cells.